

SUBJECT: VACCINE INVESTMENT STRATEGY

Agenda item: 08

Category: For Decision

Section A: Introduction

- The purpose of this report is to present the final investment cases for the six shortlisted vaccines for endemic disease prevention in the Vaccine Investment Strategy (VIS) 2018. These six vaccines are: diphtheria, pertussis & tetanus-containing (D,T&P containing) boosters; hepatitis B birth dose; A, C, W-containing multivalent meningococcal conjugate vaccines; oral cholera vaccine (OCV); rabies post-exposure prophylaxis (PEP); and respiratory syncytial virus (RSV) immunisation products.
- This report covers the vaccines for endemic disease prevention only; inactivated polio vaccine (IPV)¹ and pandemic influenza are addressed in Docs 12 and 13, respectively.
- The Board is asked to:
 - Approve an extension of Gavi support for use of the global cholera stockpile in endemic settings for 2020; and a learning agenda for oral cholera vaccine in 2019-2020. The financial implications are approximately US\$ 43.5 million for 2019-2020.
 - Approve investment in the six VIS vaccines with programmes beginning in the next strategic period (i.e. 2021), contingent upon sufficient funding being available for the 2021-2025 period and subject to the final parameter setting for Gavi 5.0 at the June 2019 Board meeting. Learning agenda activities for the five vaccines beyond cholera would begin subsequent to this 5.0 alignment in the second half of 2019. The financial implications are approximately US\$ 6.5 million for 2019-2020 and US\$ 373 million for 2021-2025.

Section B: Facts and Data

1. VIS methodology

- 1.1 Occurring every five years, the VIS is Gavi's prioritisation approach for new immunisation investments to inform Gavi's next strategic and funding cycle. The VIS 2018 took a differentiated approach to the candidates: a) vaccines

¹ The report on IPV includes consideration of support for whole-cell-pertussis-containing hexavalent vaccine

for endemic disease prevention, b) vaccines for epidemic preparedness and response, and c) support for a global public good vaccine, IPV, post-2020. It was conducted in three phases over 2017-2018: I) development of an evaluation framework and approach for vaccines for endemic disease prevention (November 2017); II) narrowing of these candidates to a short list, and development of an evaluation approach for vaccine investments for epidemic preparedness and response (June 2018); considerations of options for future IPV support; III) final recommendations including details on the scope and nature of Gavi's future investments (November 2018).

- 1.2 Since the last Board meeting in June 2018, the Secretariat has developed investment cases for the six short-listed vaccines for endemic disease prevention, with further analysis on programme design, financial implications to Gavi and countries and consultation with technical experts on vaccine-specific areas. As with previous phases, the Secretariat also conducted consultations with representatives of country governments and partners for insight into programmatic implementation with stakeholders from 17 Gavi-supported countries interviewed individually or in small groups. An on-line survey was also disseminated and received 96 responses. Members of 16 Board constituencies and seats were also consulted to provide guidance on strategic issues. Finally, the VIS Steering Committee (SC) was convened to review analytical and consultative outputs and provide expert guidance on the investment cases.

2. Assessing the value of the VIS candidates

- 2.1 The VIS 2018 candidate vaccines for endemic disease prevention were rigorously assessed in phase II, and all demonstrated compelling **health impact** and **value for money**. Some of them are viewed as high priority in specific regions and countries (e.g. high burden of meningococcal disease and cholera where they occur). Other vaccines were prioritised across Gavi-supported countries in consultations (i.e. D,T&P-containing boosters, hepatitis B birth dose). Some of the vaccines were also seen to have a strong fit with Gavi's objective to support countries to accelerate access to new and underutilised vaccines (e.g. RSV and rabies).
- 2.2 The VIS vaccines also add value to Gavi's portfolio in a number of ways:
 - a) **Closing the immunity gap and increasing impact:** Hepatitis B birth dose provides early protection between birth and the first dose of pentavalent vaccine, which is particularly important as perinatal infections have a higher risk of developing into chronic hepatitis B infection. D, T, &P-containing boosters confer longer-term protection by addressing the waning immunity of the primary pentavalent series. Multivalent meningococcal expands serogroup protection beyond NmA (covered in the currently supported MenAfriVac) to address incidence of serogroups C and W, and potentially other emerging serogroups. These vaccines would add to the already high impact from Gavi's current pentavalent and meningococcal vaccine investments.

- b) **Protecting vulnerable populations and equitable access:** Rabies vaccine would protect those who have historically been unable to access vaccine from a 100% fatal disease. Oral cholera vaccine would reduce incidence and transmission of a disease that mainly affects the poor and marginalised. RSV immunisation products could reduce the mortality in neonates, and Gavi support would ensure lower income countries access the vaccine with no delay compared to high income countries. PPC members agreed that support for these vaccines would align with Gavi's mission of increasing equitable access and uptake.
- c) **Reducing outbreaks and antimicrobial resistance:** Pre-emptive cholera vaccination and routine immunisation with multivalent meningococcal vaccine could prevent costly and disruptive outbreaks of these diseases and reduce reliance on the stockpiles for outbreak response, while D, T&P-containing booster vaccination could protect vulnerable populations against increasingly frequent diphtheria outbreaks. RSV and meningococcal vaccination would reduce the incidence of infections and the ensuing use of antibiotics to treat them, thereby potentially reducing contribution to antimicrobial resistance.
- d) **Integrating a life-course perspective to improve coverage and equity and strengthen Primary Health Care (PHC):** Several VIS vaccines reflect a global trend in immunisation of moving beyond a traditional focus on infants, toward an approach of protecting health along the life-course (e.g. vaccinating at birth, 2nd year of life, school entry, adolescence, pregnancy). Establishing or strengthening these new time-points to deliver the VIS candidates can also be leveraged to improve the uptake and coverage of existing vaccines (e.g. measles, HPV) and could help with introduction of future vaccines (e.g. TB). As these time-points are also critical for delivery of other health interventions (e.g. antenatal care, skilled birth attendance, newborn care, growth monitoring, nutrition supplementation, sexual and reproductive health), and immunisation already has the highest coverage rate among all PHC interventions, this would be an opportunity to further leverage the immunisation platform to strengthen PHC, and potentially help to achieve synergies across different components of health service delivery. The PPC was broadly supportive of a life-course approach but suggested development of Gavi's 2021-2025 strategy appropriately consider how these vaccines align with Gavi's broader role in supporting the SDGs and UHC (see Doc 11 for discussion of Gavi's role in the next strategic period).

3. Enhancing country ownership

- 3.1 While most of the six VIS vaccines are relevant across countries, consultations highlighted that each represents different degrees of value and impact at an individual country level (e.g. based on local disease burden). This provides an opportunity to further evolve Gavi's portfolio towards greater country choice. Countries could more proactively identify a customised mix of vaccines from the portfolio to introduce, taking into

account their needs and capacities as well as other priorities, for maximum value in their context. This would facilitate greater flexibility for countries and strengthen country-driven decision-making.

- 3.2 Strengthened decision-making capacity and tools (e.g. NITAGs) and a strong evidence base, in particular on disease burden, would be critical for countries to make informed choices, requiring investments in surveillance and improved data quality. Partners such as WHO would be critical to provide technical guidance, such as a framework to facilitate consistent, evidence-based prioritisation.

4. Enabling successful uptake of VIS vaccines

- 4.1 *Collaborating for synergy.* For some VIS vaccines (e.g. cholera, rabies), immunisation is one crucial intervention in increasingly multisectoral approaches to disease control. Immunisation can be a lever to bring attention to other needed interventions; to achieve the intended impact, Gavi would need to collaborate with other stakeholders with experience in non-immunisation interventions (e.g. water, sanitation and hygiene [WASH] for cholera; dog vaccination for rabies), as these activities lie outside its remit. Other VIS vaccines (e.g. maternal RSV, hepatitis B birth dose) are delivered through broader health service delivery platforms, such as antenatal and post-natal care. Alignment between Gavi and maternal and child health stakeholders could maximise their impact. The PPC proposed that as Gavi considers its role in the next strategic period within the broader integration agenda, all stakeholders are clear on accountability and responsibilities.

- 4.2 *Learning and improving.* Given the different nature of the VIS vaccines (e.g. the establishment of new time-points or need to integrate across sectors for broader disease control), a number of programmatic and operational questions remain. Answering some of these questions would address gaps in knowledge relevant for optimal programme design and enhance the impact of Gavi's investment. A VIS learning agenda would address three main areas: generate disease burden evidence to inform programme implementation and impact assessment; design impactful and feasible programmes and delivery strategies; apply learnings from initial roll-out of a Gavi programme to improve uptake and coverage. Specific questions for the VIS learning agenda would be developed in consultation with stakeholders after a review of the most relevant and critical strategic questions for Gavi.

5. VIS in the context of Gavi's 5.0 strategy

- 5.1 The PPC reflected that given the similarities and differences of VIS vaccines compared to the current portfolio, it would be essential that development of Gavi's 2021-2025 strategy consider the fit and potential support for these vaccines. As Gavi identifies the key principles and goals for the next strategic period, the Secretariat will consider key questions posed by the VIS, alongside the current portfolio, with implications for its mandate and

operating model: How could Gavi consider support for successful introduction of new vaccines to complement efforts to strengthen coverage and equity (e.g. through health systems investments)? How should Gavi support for vaccines, including those delivered at new time-points, be considered as a part of tailored and differentiated programmatic approaches that better adapt to each individual country situation? What other aspects of Gavi's support model (beyond financial support) could evolve with inclusion of the VIS vaccines in Gavi's portfolio (e.g. Gavi's role in gender equity vis-à-vis neonatal and maternal immunisation, antimicrobial resistance)? How should Gavi approach collaboration with other key global health stakeholders to leverage the immunisation platform to contribute to stronger PHC and UHC (e.g. for developing collaborative and impactful approaches to integrated disease control and health promotion)?

- 5.2 To address these questions, the 5.0 approach will assume inclusion of the VIS vaccines in Gavi's portfolio. Multiple scenarios of vaccine portfolios would not be specifically detailed out, given the complexity taking into account the number of other themes, strategic shifts, and objectives. However, the implications and costs of the VIS vaccines will be clearly noted to inform decision-making.

6. Investment cases for vaccines for endemic disease prevention

- 6.1 Full investment cases for each vaccine can be found in Appendix 2 and summaries and overall costs and health impact in Annex B.² Investment in hepatitis B birth dose and D, T &P-containing booster vaccines would be catalytic support to overcome introduction barriers and establish and strengthen the immunisation timepoints, as these vaccines are inexpensive and fall below the threshold for Gavi vaccine support. Investment in meningococcal conjugate vaccines and RSV immunisation products would be based on future availability of appropriate products and WHO recommendations.
- 6.2 The PPC was broadly supportive of all of the candidates, noting their relevance for Gavi-supported countries and the potential role Gavi could play in accelerating their uptake. Given the links to development of Gavi's next strategy, the PPC recommended that the decision to approve the investments be contingent on the final parameters set within the strategy at the June 2019 Board meeting. However, to prevent disruptions and to optimise Gavi's existing cholera programme, the PPC recommended the Board approve funding for 2020 to extend the current cholera investment and support a learning agenda. All other programmes would be expected to begin in 2021³ following replenishment and availability of suitable products, with the VIS learning agenda commencing after the outcomes of the June 2019 Board meeting.

² Malaria was also assessed but only as a comparator to other VIS candidates, and continues to show good value for money and impact compared to other candidates.

³ Programme commencement is contingent on sufficient funding raised through replenishment, at which point funding-related policies would be updated, and will reflect any changes needed to be fit for purpose for both the current portfolio and the VIS vaccines.

7. Financial implications

- 7.1 The costs described in each individual vaccine investment case reflect an ‘unconstrained’ scenario in which introductions were forecasted as if only that specific vaccine were added to Gavi’s portfolio. However, both financial and programmatic capacity constraints would limit countries’ introduction of VIS vaccines if all were options for introduction, so these individual cost projections cannot simply be aggregated.
- 7.2 To account for this, the aggregated cost projection was adjusted to derive an estimate for the portfolio of six VIS vaccines. The pace of vaccine introductions and campaigns (across both current portfolio and VIS) was adjusted to align the total introductions in future strategic periods with the historical pace of introductions observed.⁴ Using this methodology, the costs to Gavi of supporting the portfolio of six VIS candidates as a whole are estimated to be approximately US\$ 360 million for the 2021-2025 period.⁵ Details on the costs and impacts of the portfolio of six vaccines can be found in Annex B, alongside further description of the learning agenda.
- 7.3 The financial implications of the VIS learning agenda (excluding cholera) and RSV introduction planning activities is projected to be US\$ 19.5 million from 2019-2025, of which US\$ 6.5 million is associated with the 2019-2020 period and US\$ 13 million is for 2021-2025. For 2019, resources will be managed within the existing approved budget, while for 2020 and beyond, resourcing would be addressed as part of the regular budgeting process.
- 7.4 The financial implications for extending the use of the cholera vaccine stockpile for endemic settings in 2020 and the cholera learning agenda for 2019-2020 is projected to be US\$ 43.5 million.
- 7.5 The VIS Steering Committee noted that capacities within countries, the Secretariat and Alliance partners would need to evolve and expand in order to enable decision-making on introduction of VIS vaccines, as well as the associated delivery platform establishment. The indicative cost projections outlined above exclude potential financial implications for the Secretariat and partners for human resources. For 2019, Secretariat and partner resources will be managed within the existing approved budgets. For 2020 and beyond, resourcing would be addressed as part of the regular budgeting process.

Section C: Actions requested of the Board

The Gavi Alliance Programme and Policy Committee recommends to the Gavi Alliance Board that it, subject to the availability of funding for the 2021-2025 period following Gavi’s replenishment for that period and subject to alignment with the final parameter setting for Gavi 5.0 at the June 2019 Board meeting:

⁴ Based on actual and forecasted introductions of current portfolio vaccines

⁵ Inclusive of vaccine procurement and operational cost support

- a) **Approve** support for diphtheria, tetanus & pertussis-containing (D, T & P) vaccines (tetanus-diphtheria, diphtheria-tetanus-whole-cell pertussis, pentavalent) to be used as booster doses beginning in 2021 by:
 - i. Providing funding to establish platforms as catalytic support for the introduction of each D, T, & P-containing vaccine as a booster dose;
 - ii. Supporting the procurement of above mentioned D, T, & P-containing booster vaccines in line with the co-financing policy.
- b) **Approve** support for hepatitis B birth dose beginning in 2021 by:
 - i. Providing funding to establish platforms as catalytic support for the introduction of hepatitis B vaccine administered at birth
 - ii. Supporting the procurement of hepatitis B vaccines in standard vial presentations and in line with the co-financing policy.
- c) **Approve**, in principle, an expansion of the existing meningococcal programme to support a targeted approach that includes, in principle, support for ACW-containing multivalent meningococcal conjugate vaccines, contingent on the availability of a licensed product, outcomes of regulatory and technical review processes (including WHO prequalification and SAGE recommendation) and meeting the financial assumptions used as the basis for the multivalent meningococcal vaccine investment case set out in Doc 08 Appendix 2.
- d) **Approve** a transition of the oral cholera vaccine programme to include a preventive immunisation programme with vaccine co-financing, beginning in 2021.
- e) **Approve** support for human rabies vaccine for post-exposure prophylaxis, beginning in 2021.
- f) **Approve**:
 - i. In principle, support for Respiratory Syncytial Virus (RSV) immunisation products, contingent on the availability of a licensed product, outcomes of regulatory and technical review processes (including WHO prequalification and SAGE recommendation), and meeting the financial assumptions used as the basis for the RSV investment case set out in Doc 08 Appendix 2.
 - ii. Support beginning in 2019 for pre-introduction activities for RSV immunisation products including evidence and demand generation.
- g) **Approve** the VIS learning agenda for 2019-2025 for D, T & P-containing booster vaccines, hepatitis B birth dose, ACW-containing multivalent meningococcal conjugate vaccines and human rabies vaccine for post-exposure prophylaxis, as described in Doc 08 Annex B.

- h) **Note** that the financial implications associated with the above conditional approvals for 2019-2020 are expected to be approximately US\$ 6.5 million, comprised of approximately US\$ 3 million in 2019 (which the Secretariat will strive to absorb from the Board-approved PEF budget for that year) and US\$ 3.5 million in 2020 for the VIS learning agenda for the vaccines described above and RSV introduction planning activities.
- i) **Note** the financial implications associated with the above conditional approvals (taken as a whole) for 2021-2025 for vaccine and operational cost support are expected to be approximately US\$ 373 million, comprised of approximately US\$ 360 million for vaccine and operational cost support and approximately US\$ 13 million for the VIS learning agenda and RSV introduction planning activities.

The Gavi Alliance Programme and Policy Committee recommends to the Gavi Alliance Board that it:

- a) **Approve** an extension of Gavi support for use of the global cholera stockpile in endemic settings for 2020, whereby components of the preventive immunisation programme are implemented beginning in 2019.
- b) **Authorise** the Secretariat, under the Programme Funding Policy, to (i) allot funding to the global cholera stockpile based on a financial forecast endorsed by the Board, (ii) allot funding to extend budgets to future years and/or (iii) adjust annual budget amounts as authorised by the CEO/DCEO taking into account updated timing of implementation and budget utilisation;
- c) **Approve** the VIS learning agenda activities for cholera for 2019-2025 as described in Doc 08 Annex B; and
- d) **Note** that the financial implications associated with the above approvals for 2019-2020 are expected to be approximately US\$ 43.5 million, comprised of approximately US\$ 0.5 million in 2019 (which the Secretariat will strive to absorb from the Board-approved Partners' Engagement Framework (PEF) budget for that year) and US\$ 1 million in 2020 for the VIS learning agenda for cholera, and US\$ 42 million for extension of cholera support in 2020.

Annexes

Annex A: Implications/anticipated impact

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

Additional information available on BoardEffect

Appendix 1 (in October 2018 PPC meeting book): Annex B to Doc 06a *VIS Phase III stakeholder engagement*

Appendix 2 (in October 2018 PPC meeting book): Annex C to Doc 06a Investment cases for each of the six candidate vaccines for endemic disease prevention

Appendix 3 (in PPC Library – Additional materials for October 2018 meeting): Appendix 1 to Doc 06a *Summary of VIS Phase III country consultations*

Appendix 4 (in PPC Library – Additional materials for October 2018 meeting): Appendix 2 to Doc 06a *Summary of key VIS Phase III analysis outcomes for vaccines for endemic disease prevention*

Appendix 5 (in PPC Library – Additional materials for October 2018 meeting): Appendix 3 to Doc 06a *Malaria vaccine analysis*

Additional reference materials online:

VIS internet page: <http://www.gavi.org/about/strategy/vaccine-investment-strategy/>