Subject	**Respiratory Syncytial Virus (RSV) Investment Case**
Agenda item	**08**
Category	**For Decision**

Executive Summary

Respiratory Syncytial Virus (RSV) is the leading cause of pneumonia and infant hospitalisation, and the second leading etiology of infant deaths. In 2018, Gavi's Board approved, in-principle, through the Vaccine Investment Strategy (VIS), RSV immunisation products contingent on key conditions, now met with a licensed, WHO-prequalified, and SAGE-recommended maternal RSV vaccine to protect infants, with its manufacturer committed to offering terms for Gavi access.

The purpose of this paper is to present an update on RSV's high burden, the vaccine's health and economic impact, and request Board approval to open a funding window for a potential RSV maternal vaccine programme.

This investment case was informed by guidance from an RSV Working Group with representatives from partners including WHO, UNICEF, Africa Centres for Disease Control (CDC), the Gates Foundation, and consultations with countries, independent experts, and vaccine manufacturers.

Action Requested of the Board

The Gavi Alliance Programme and Policy Committee **recommended** to the Gavi Alliance Board that, contingent on financial resources being made available for the Gavi 6.0 strategic period, it:

a) **Approve** the opening of a funding window for the establishment of an RSV maternal vaccine programme to protect infants;

b) **Note** that the initial cost estimates associated with the above approval for the period 2026-2030 are US$ 14.8 million. Future financial forecasts will reflect potential changes in the underlying assumptions of these estimates.

Next steps/timeline

If approved, taking into consideration any potential recalibration of Gavi 6.0 priorities by the Board and contingent on financial resources being made available, Gavi would begin a 12–18-month planning phase to co-develop implementation strategies with partners and launch a market shaping roadmap. With WHO prequalification of the multidose vial expected by late 2026, the first application window could open in late 2027, with introductions starting in 2028.

Previous Board Committee or Board deliberations related to this topic

In May 2025 PPC folder: Doc 16 - *Respiratory Syncytial Virus (RSV) Investment Case*

In May 2023 PPC folder: Doc 08 - *Vaccine Investment Strategy 2018*

In November 2018 Board meeting book: Doc 08 - *Vaccine Investment Strategy*

Report

1. Background and decision history

1.1 Respiratory Syncytial Virus (RSV) is the leading cause of pneumonia in children, responsible for most hospitalisations due to lower respiratory tract infections (LRTIs) globally, in the era of broadscale use of Pneumococcal Conjugate Vaccine (PCV) and Haemophilus influenzae type b (Hib) vaccine[1]. Each year, RSV causes approximately 33 million cases of LRTIs and 3.6 million hospitalisations among children under five, with the highest burden in the first year of life[2]. RSV is also the second leading cause of infant mortality after malaria, with an estimated 101,400 directly attributed annual deaths in children under five, half of which occur in infants younger than six months. In addition, over 97% of these deaths occur in low- and middle-income countries (LMICs), with the highest impact in Africa. Alarmingly, 50-80% of RSV-related deaths occur outside hospital settings[3], underscoring inequities in healthcare access.

1.2 RSV immunisation products to protect infants, a maternal vaccine and a long-acting monoclonal antibody (mAb), were approved in-principle through Gavi's Vaccine Investment Strategy (VIS) 2018 due to their significant potential to avert disease burden, particularly in Gavi-supported countries. Gavi's role in shaping the market and ensuring equitable access to the vaccine aided in this decision. However, this initial decision was accompanied by many uncertainties due to the lack of licensed products at the time.

1.3 The Board's in-principle decision in 2018 was contingent on key conditions: the availability of a licensed product, regulatory and technical approvals (including World Health Organisation (WHO) prequalification (PQ) and recommendations from the Strategic Advisory Group of Experts on Immunization (SAGE), and validation of financial assumptions underpinning the RSV investment case. During the COVID-19 pandemic, the Board decided to pause the rollout of some of the VIS 2018 vaccines. The Programme and Policy Committee (PPC) in May 2023 provided guidance to resume previously paused decisions and begin programme design. The RSV programme is now the last remaining initiative from the VIS 2018 decisions to be potentially included in the portfolio.

1.4 The RSV maternal vaccine to protect infants has now met the original investment conditions for opening a funding window outlined above. Moreover, updated studies on disease burden and the product's characteristics regarding efficacy, duration of protection, and price, reinforce RSV's prevention potential impact and cost-effectiveness.

1.5 In May 2025, the PPC expressed strong support for the introduction of the RSV maternal vaccine and requested that it be recommended to the Board for

[1] O'Brien K, et al. Lancet. 2019.
[2] Li Y, et al. Lancet. 2022.
[3] Srikantiah P, et al. *Clin Infect Dis* 2021.

approval at its July 2025 meeting. The PPC urged the Secretariat to expedite programme planning and to accelerate the vaccine's introduction timeline.

2. Key updates since the VIS 2018 decision

2.1 **Increased RSV mortality and improved surveillance:** Updated global estimates of RSV burden of disease reconfirm the burden documented for VIS 2018. However, new evidence reveals that out-of-hospital RSV deaths among young infants in Low-Income Countries (LICs) are likely four times higher than previously estimated, reflecting improved surveillance and its true burden[4,5].

2.2 **Availability of licensed RSV immunisation products**: Since 2018, two RSV immunisation products to protect infants have been broadly licensed, recommended by SAGE and WHO for global use, and introduced in several high- and upper middle-income countries. Additionally, PAHO's Revolving Fund has made the maternal vaccine available in the region, the European Technical Advisory Group of Experts (ETAGE) has recommended these products and the African Regional Immunisation Technical Advisory Group (RITAG) is set to discuss a potential recommendation in June 2025[6].

2.2.1 **Maternal vaccine to protect infants** (Abrysvo, Pfizer): Administered in the third trimester of pregnancy, this single-dose vaccine boosts pre-existing antibodies in the mother and hence provides passive immunity and protection to the newborn through maternal antibodies. While the phase 3 clinical trial observed a non-significant imbalance in preterm births (with risk lower than the general population), a 2024 safety review by WHO's Global Advisory Committee on Vaccine Safety (GACVS) found no statistical significance or biological mechanism of concern. In addition, SAGE reviewed post-authorisation data from the US, confirming no increased prematurity risk.

2.2.2 **Long-acting monoclonal antibody (mAb)** (Nirsevimab-Sanofi/AstraZeneca): Administered at birth or during the first few weeks of life in a single-dose schedule, the mAb provides passive immunisation during the first 6 months of life. Clinical trials and early introductions showed an overall favourable safety profile and co-administration with childhood vaccinations.

2.3 **Provision of SAGE & WHO recommendation:** In September 2024, SAGE recommended that all countries introduce passive immunisation to prevent severe RSV disease in young infants. Countries should choose between the maternal vaccine and/or the long-acting monoclonal antibody based on cost, financing, supply, anticipated coverage, and feasibility of implementation within the existing health system[7].

2.4 **WHO-prequalification:** In March 2025, WHO prequalified the single-dose vial (SDV) presentation of the maternal vaccine, making it the first WHO-

[4] Srikantiah P, et al. *Clin Infect Dis* 2021.
[5] https://www.who.int/news-room/fact-sheets/detail/respiratory-syncytial-virus-(rsv)
[6] https://www.paho.org/en/news/1-11-2024/
[7] https://www.who.int/publications/i/item/who-wer-10022-193-218

prequalified product to prevent RSV[8]. Prequalification of a multidose vial (MDV) presentation of Abrysvo, specifically targeted for the LMIC market, and identified as the formulation for potential Gavi support, is expected in 2026.

2.5 **Access commitment:** Based on ongoing market shaping engagement to support long-term planning and alignment of VIS assumptions, the manufacturer is committed to offering terms for Gavi access (for the MDV presentation) which will allow delivery of the programme within the funding envelope assumed in the initial VIS 2018 investment case.

3. Updated investment case

3.1 An updated investment case for the RSV maternal vaccine to protect infants was developed and informed by extensive engagement with global health and country-level stakeholders, and developed following Gavi's VIS methodology and key assumptions detailed in Annex B.

3.2 This investment case focuses on the **maternal vaccine to protect infants** due to the high cost of the monoclonal antibody (mAb) currently licensed in high and middle-income countries (~US$ 200–520 per dose). Potentially more affordable mAbs are in the pipeline, including Clesrovimab (Merck), which was recently licensed, with its earliest prequalification likely not before 2029.

3.3 A revised **demand forecast** was developed incorporating expert input. While uncertainties remain on demand materialisation, emerging evidence supports a robust forecast[9,10,11]. The baseline demand scenario projects seven countries will introduce the RSV maternal vaccine during Gavi's 6.0 strategic period, with the first country introduction in 2028. The estimated range varies from three to eleven countries. The forecast was input to generate estimates for costs, impact, and value for money.

3.4 Compared to other Gavi-supported vaccines, the RSV maternal vaccine is projected to deliver a strong **health impact** (Table 1) and falls within Gavi's portfolio range of cost effectiveness (Annex B). With a longer duration of protection, higher burden estimates, improved efficacy, and reduced costs, the estimated impact and cost-effectiveness of the RSV maternal vaccine are now greater than previously assessed in VIS 2018.

[8] https://extranet.who.int/prequal/vaccines/p/abrysvo
[9] The Maternal Immunisation Readiness Network in Africa and Asia (South Africa, Bangladesh, Burkina Faso, Ethiopia, Ghana, Kenya, Nigeria, Pakistan, Uganda) actively preparing for RSV maternal vaccine implementation
[10] Afro RITAG is set to discuss a potential recommendation in June 2025 for all countries on RSV products.
[11] WHO's global list of priority endemic pathogens, identified through regional surveys, RSV as a high-priority pathogen, urging countries to prepare for introduction. Mateusz Hasso-Agopsowicz, et al. eBioMedicine 2024.

3.5 **Table I:**

		6.0 (2028-2030)	**7.0** (2031-2035)	**8.0** (2036-2040)	**Total**
Health impact	Total severe cases averted	166K	1M	2.2M	3.4M
	Total deaths averted	6.9K	60.8K	141K	209K
	Total future DALYs averted	613K	5.4M	12.6M	18.6M
Value for money	Gavi cost / Total cost per death averted (US$)	2.2K / 4.8K	1.4K / 3.8K	1.1K / 3.8K	1.3K/3.8K
	Gavi cost / Total cost per DALY averted (US$)	24.2 / 54.3	16.2 / 43.1	12.8 / 42.6	14.1/43.1

3.6 RSV prevention strategies are anticipated to confer broad protective effects beyond RSV-specific illness, including reductions in all-cause and recurrent LRTIs, thereby supporting improved pulmonary health trajectories throughout early childhood. Beyond the health impact, RSV places a significant economic burden on health systems and households due to high hospitalisation rates and oxygen dependency[12]. Reducing severe hospitalised RSV cases would free up critical hospital capacity. In addition, RSV prevention lowers overall antibiotic use.

4. Strategic alignment and opportunities

4.1 Supporting the RSV maternal vaccine aligns with Gavi's 6.0 vision and mission by enabling its introduction in high-burden, Gavi-eligible countries, while also advancing global health goals, including Sustainable Development Goal 3. RSV prevention also complements Gavi's existing pneumonia prevention efforts.

4.2 Strengthening maternal immunisation platforms for RSV could also pave the way for future vaccines, such as Group B streptococcus, which the Board approved in principle in June 2024 as part of VIS 2024.

5. Implementation feasibility

5.1 The RSV maternal vaccine can be delivered through Antenatal Care (ANC) or the Expanded Programme on Immunization (EPI). While maternal vaccination is a new delivery point for Gavi, it builds on an established platform in Gavi-supported countries, particularly through tetanus immunisation efforts[13]. Most pregnant women attend at least four ANC visits (median 73%, interquartile range (IQR) 64-76).

[12] Lewnard JA, et al. PNAS. 2022.
[13] Median tetanus toxoid coverage at 63% (IQR 44-86) in Gavi 54 countries, with 45 having achieved Maternal Neonatal Status Elimination over last 25 years.

5.2 RSV immunisation depends on a well-functioning ANC platform, but it can also strengthen it - by integrating into ANC services, it reinforces both EPI and broader maternal, newborn, and child health (MNCH) efforts.

5.3 Despite this strong foundation, ANC investing remains a continuous need, as it is essential for reaching women at the right time during pregnancy and to ensure the successful implementation of RSV maternal immunisation. With varying levels of ANC service coverage across Gavi-supported countries, additional outreach and alternative delivery models may be required to achieve high coverage beyond what is expected from ANC, which was used as a proxy in the investment case. Recent cuts in donor funding for maternal health and ANC services may worsen these challenges, potentially weakening service delivery and limiting vaccine access.

6. Market shaping considerations

6.1 Although this market is expected to be "single supplier" for the near to mid-term, no market shaping challenge has been identified as the supplier is well-established with a reliable track record and has offered an access commitment for the product in LMICs. The supplier has already secured WHO-prequalification for its SDV presentation, and its MDV presentation, more suitable for Gavi-supported countries, is on track for WHO-prequalification by the end of 2026.

6.2 However, there is an important need to clarify the magnitude of the potential Gavi demand as soon as possible to ensure the manufacturer can plan capacity to align with the expected materialisation of demand and have MDV supply ready for 2028.

7. Financial impact

7.1 **Total procurement costs** were calculated using demand and price forecasts, applying Gavi's Co-financing and Eligibility and Transition policies to determine costs for Gavi and countries[14]. **Total vaccine delivery costs** through ANC were estimated using the best available maternal immunisation data costing from Gavi-supported countries. Based on these estimates, the expected delivery cost shares for countries and Gavi were then determined. For Gavi 6.0, Gavi delivery costs were estimated using cash-related support for introduction[15], which will be translated into the country Gavi 6.0 consolidated cash envelopes[16] once a vaccine programme is launched.

7.2 **For Gavi:** The associated costs for the introduction of the RSV maternal vaccine are US$ 14.8 million in Gavi 6.0 (US$ 10.3 million for vaccines and ancillary costs and US$ 4.5 million for cash-related support for introduction under the baseline demand scenario of 7 early adopter countries introducing in

[14] Vaccine costs are based on a fully loaded vaccine price, costs of freight, safety boxes, and syringes.
[15] Cash-related support for introduction was estimated using Vaccine Introduction Grant (VIG) costs as per Gavi's current Vaccine Funding Guidelines – VIGs will be consolidated into one cash support envelope in Gavi 6.0.
[16] During Gavi 6.0, countries will be required to prioritise their consolidated cash envelope towards vaccine introduction support, delivery support through health system strengthening, and technical assistance.

Gavi 6.0). This is consistent and results in lower costs compared to the Gavi 6.0 costing exercise and the initial VIS 2018 expectations.

7.3 The expected costs in future strategic periods will depend on country demand and the level of ambition defined for the programme. In Gavi 7.0, the total costs expected are US$ 87.4 million, comprising US$ 69 million for vaccines and ancillary costs and US$ 18.3 million for cash-related support for introduction, assuming 23 new countries introducing. In Gavi 8.0, the total costs expected are US$ 152 million for vaccines and ancillary costs and US$ 8.3 million for cash-related support for introduction, assuming 7 new countries introducing.

7.4 **For countries:** Aligned with Gavi's policy, countries will be expected to co-finance routine doses for the RSV maternal vaccine. The co-financing impact for countries is estimated at US$ 6.2 million in Gavi 6.0. The procurement cost for countries is US$ 44 million in Gavi 7.0 and from US$ 102 million in Gavi 8.0. The expected country share of delivery costs is US$ 12.2 million, US$ 101 million, and US$ 273 million for Gavi 6.0, 7.0, and 8.0, respectively.

8. Next steps

8.1 If approved and contingent on financial resources being made available, Gavi would initiate a 12-18-month programme planning phase, co-developing implementation strategies with partners and launching a market shaping roadmap to guide procurement and market dynamics. With WHO prequalification of the MDV expected by late 2026, the first application window could open in late 2026 or early 2027, with country introductions beginning in 2028 - or optimistically in late 2027.

8.2 For infant mAbs, the Secretariat will continue analysis and manufacturer engagement, bringing a follow-up recommendation to the PPC and Board once investment conditions are met and the use case for Gavi-supported countries is clearer.

Annexes and Appendices

Annex A: Implications and Anticipated Impact

Annex B: Respiratory Syncytial Virus (RSV) Investment Case

Additional information available on BoardEffect

Appendix 1: Supplementary Information