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| Subject | Vaccine Investment Strategy 2024: longlist and evaluation frameworks |
| Agenda item | 09 |
| Category | For Decision |

Section A: Executive Summary

Context

The Vaccine Investment Strategy (VIS) is Gavi's prioritisation process to evaluate vaccines and immunisation products for inclusion into the portfolio. Every 5 years, through this rigorous, consultative and transparent process, the Secretariat reviews evidence and carries out impact modelling to identify and assess new and/or under-used vaccines of high public health relevance for Gavi-eligible countries. The VIS facilitates strategic decision-making and provides predictability to countries, manufacturers, and donors for their own planning and future decision-making. It is a fundamental tool in fulfilling Gavi's aim of shortening the time between life-saving vaccines being available in high-income countries to them being rolled out in lower income countries.

This paper seeks Board approval on the first step in the VIS 2024 process: vaccine candidate longlist and evaluation frameworks to assess them against. There will be two more governance decision points related to the VIS: **a) Board December 2023** will consider a shortlist of vaccines; and **b) Board June 2024¹** will make final decisions on investment cases into new routine/ preventive vaccination programmes, stockpiles, or learning agendas for implementation in Gavi 6.0, subject to a successful replenishment cycle.

The VIS draws on the expertise of Alliance partners and other stakeholders to reflect multidisciplinary perspectives. An independent VIS Steering Committee² has been convened to provide technical and scientific guidance to the Secretariat in advance of governance decision points, and country input was sought during this first phase through a non-representative survey that received 111 responses from 36 Gavi countries.³

As part of the VIS 2024, the Secretariat proposes to evaluate the potential of providing support to develop, strengthen and deliver vaccines at new touchpoints for specific target populations (i.e. health workers and pregnant people), building upon lessons learned related to the relaunch of HPV, introduction of malaria and delivery of COVID-19 vaccines, which required additional support to ensure sustainability and

¹ VIS 2024 is in close alignment with the development of the Gavi 6.0 strategy to ensure that the outcomes of VIS 2024 respond to and inform the strategic priorities defined in Gavi 6.0, which will also be reviewed by the Board in June 2024.

² Steering Committee members and summaries from meetings (Dec 2022, Apr 2023) in Appendix 1.

³ The survey took place in March 2023 and targeted government officials (Ministry of Health, EPI managers, and other ministries) and in-country Gavi Alliance partners. Result summary in Appendix 2.

coverage beyond introduction, and in anticipation of future vaccines to be delivered at these timepoints.

Questions this paper addresses

- What pathogens should be included in the VIS 2024 vaccine longlist?
- How should the vaccines in the longlist be evaluated?
- Should the VIS 2024 consider the potential value of supporting immunisation platforms for specific populations (e.g. health workers, pregnant people)?

Conclusions

Based on PPC recommendations, this paper presents for Board approval: a) a proposed longlist of pathogens (hepatitis E, m-pox, dengue, COVID-19, tuberculosis, group B streptococcus, chikungunya, and shigella) for more in-depth analyses; and b) the evaluation frameworks that will be used for these analyses including criteria and indicators. It also proposes to use the VIS 2024 as an opportunity to consider the potential value of supporting immunisation platforms for specific populations. These proposals have received input from experts, technical partners and Gavi countries.

Section B: Facts and Data

1. Introduction

- 1.1 The Secretariat carries out the VIS every 5 years to inform Gavi's five-year strategy development and subsequent replenishment efforts, and provide predictability to countries, manufacturers, and donors for their own planning and future decision making. Gavi launched its fourth VIS (2024) in January 2023 with a Technical Briefing to PPC and Board members. VIS 2024 aims to inform investments for Gavi 6.0 (2026-2030).
- 1.2 The process starts with the identification of which vaccines will be evaluated (the vaccine longlist) and how (the evaluation frameworks), this first step is the focus of this paper. Subsequent analytical review of evidence and impact modelling based on data inputs such as the burden of disease, vaccination strategies, demand in countries, feasibility of implementation and cost will be used to project potential impact over the coming strategic period to compare and evaluate trade-offs between potential vaccine investments.
- 1.3 The VIS can evaluate vaccines against endemic and epidemic pathogens, using two different evaluation frameworks. Gavi can also evaluate and develop vaccine investment cases for epidemic diseases in real-time when an immediate decision is required outside the 5-year VIS cycle, in response to a public health threat (e.g. recent m-pox and Marburg outbreaks) or when a vaccine R&D milestone is achieved for a priority epidemic pathogen as defined by the WHO R&D Blueprint priority diseases.⁴

⁴ WHO's R&D Blueprint is a global strategy and preparedness plan that allows the rapid activation of R&D activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used

1.4 The VIS process results in a global prioritisation of vaccine candidates for Gavi’s portfolio with input received through consultations with countries (e.g. survey) and experts (e.g. VIS Steering Committee). Ultimately, countries will decide through their national-level process whether they wish to prioritise a vaccine or not based on their context, once Gavi makes a vaccine application window available.

2. VIS 2024 vaccine longlist

2.1 The VIS 2024 vaccine longlist has been informed by a landscape analysis carried out by WHO’s Immunization, Vaccines and Biologicals (IVB) Department leveraging expert advice from the Product Development for Vaccines Advisory Committee (PDVAC) and based on the following primary inclusion criteria: a) vaccines and passive immunisation products (e.g. antibodies) of relevance to Gavi countries with expected licensure by 2030 and a pathway to a SAGE policy recommendation; and b) licensed vaccines and passive immunisation products of relevance to Gavi countries not currently in Gavi’s portfolio.

2.2 Following consultations with the VIS Steering Committee, other partners and further refinement with WHO, a consolidated longlist of eight pathogens is proposed for further analysis and evaluation (see Table 1). Influenza will be considered as part of the immunisation platforms described in section 5. In addition, vaccines against Respiratory Syncytial Virus (RSV) were approved in principle as part of the VIS 2018. The lead RSV candidate has not met its primary endpoint but there are other products in the pipeline that Gavi is monitoring closely.

Table 1: VIS 2024 Vaccine longlist

| | Pathogen | Vaccine status | Target group or use | Strategic consideration and licensure/policy status and timeline for pipeline vaccines |
|---|------------------------------|--------------------|--|--|
| 1 | Hepatitis E | Licensed | Campaign/ Stockpile | <ul style="list-style-type: none"> To be evaluated as a stockpile Licensed in China 2011, policy recommendation 2015, earliest WHO PQ estimated 2028. |
| 2 | Dengue | Licensed/ pipeline | Adolescents, adults & older people | <ul style="list-style-type: none"> Market shaping opportunity. For pipeline: earliest expected licensure 2023 and policy recommendation 2024 |
| 3 | Mpox | Licensed | Campaign/ Stockpile | <ul style="list-style-type: none"> To be evaluated as a stockpile No WHO PQ, interim policy recommendation only |
| 4 | COVID-19 routine | Licensed | Older adults, health workers & pregnant people | <ul style="list-style-type: none"> As requested by Gavi Board in December 2022, for programme starting in 2026 |
| 5 | Tuberculosis | Pipeline | Adolescents, adults & older people | <ul style="list-style-type: none"> Health impact, market shaping opportunity, AMR priority Earliest expected licensure 2029 and policy recommendation 2030 |
| 6 | Group B streptococcus | Pipeline | Pregnant people | <ul style="list-style-type: none"> Market shaping signalling opportunity, AMR priority Earliest expected licensure 2028 and policy recommendation 2029 |
| 7 | Chikungunya | Pipeline | Campaign/ Stockpile | <ul style="list-style-type: none"> Pilot modelling work commissioned by Secretariat could inform evaluation. |

to save lives and avert large scale crisis. The R&D Blueprint works on the basis of a list of identified priority pathogens, that is currently under review (<https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts>).

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|---|----------|----------|----------------------|---|
| | | | | <ul style="list-style-type: none"> ▪ Earliest expected licensure 2025 and policy recommendation 2026 |
| 8 | Shigella | Pipeline | Infants and children | <ul style="list-style-type: none"> ▪ Potential benefits beyond lives saved (e.g. decrease stunting) ▪ Earliest expected licensure 2029 and policy recommendation 2030 |

2.3 The diversity of vaccine candidates reflects the evolving differentiation of Gavi's investment, from a focus on universal introductions of new and underused vaccines at Gavi's inception to investments in outbreak response, learning agendas and vaccines of regional importance. The PPC was supportive of the proposed VIS 2024 vaccine longlist.

3. Evaluation Frameworks

3.1 The VIS aims to evaluate trade-offs between vaccines and enable evidence-based decisions for strategic planning. To aid the comparative analysis, different vaccine candidates are assessed against evaluation frameworks that take into consideration the full value of vaccines beyond their impact on mortality and morbidity, to consider broader economic burden, equity and social justice, and global health security, among others. The frameworks include criteria and indicators that can be quantitative or qualitative and that are weighted differently to inform the prioritisation process.

3.2 Two frameworks will be used, one to evaluate investments in routine vaccination programmes or preventive campaigns (endemic evaluation framework) and another for investments in outbreak response (epidemic evaluation framework). Considering the final public health goal of the potential vaccine investment, four candidates will be assessed with the endemics framework (tuberculosis, group B streptococcus, dengue, shigella); and three with the epidemics framework (Hepatitis E, Chikungunya, Mpox).⁵ The evaluation approach for COVID-19 will be informed by analysis used to inform the vaccine programme for 2024-2025 (See Doc 07).

3.3 **Evaluation framework for endemic diseases:** the Secretariat reviewed the VIS 2018 framework and proposes to maintain the basic structure with *key criteria* that will be used to rank the vaccines and *modulating criteria* that may or may not be relevant for each vaccine but provide further data to inform the ultimate ranking (see Annex B to May 2023 PPC Doc 09 for details on criteria and proposed indicators).

3.4 *Key ranking criteria:* health impact identified as the most important priority by all stakeholders; value for money considering vaccine procurement cost only (other costs are considered at the investment case stage);⁶ equity, social protection in line with Gavi's mission; economic impact providing a view to the

⁵ Acute epidemic needs such as Ebola Sudan and Marburg are being considered in real-time (Paper 09).

⁶ Detailed analyses on cost implications for both Gavi and countries are carried out at the investment case stage (H1 2024) to provide a picture on financial trade-offs between vaccines. Factors such as: a) total procurement cost to Gavi and countries (2026-2030); b) operational costs – incremental in-country operational costs per vaccinated person; and c) additional implementation costs for introduction and monitoring are included and will be used to compare potential investments against each other and against vaccines currently in the portfolio.

longer-term benefits of vaccines; and Gavi's comparative advantage, which will be informed by Gavi's long horizon market shaping activities (see section 4).

- 3.5 *Modulating criteria* provide additional relevant information related to the specific vaccine. These criteria might not be relevant to every vaccine or there might not be a large amount of reliable data on them, thus they are considered to inform the ultimate ranking decision. Lack of data on modulating factors is not expected to bring the ranking of the vaccine down but may provide information that increases its ranking. These criteria include for example, global health security impact (including antimicrobial resistance – AMR), broader health systems benefit, contribution to the global agenda, alternative interventions and implementation feasibility that will inform design, implementation and costs, as well as incorporate lessons learned from the introduction and delivery of other vaccines (e.g. HPV, malaria and COVID-19).
- 3.6 The VIS Steering Committee reviewed and provided feedback on the proposed criteria and indicators, as presented in Annex B to May 2023 PPC Doc 09. The PPC was supportive of the proposed evaluation framework and its criteria and indicators, particularly of using indicators focused on Disability Adjusted Life-Years (DALYs) instead of cases.
- 3.7 **Evaluation framework for epidemic diseases:** This framework is structured around four key questions to inform future investment cases: a) disease risk and burden, b) role of vaccine, c) Gavi comparative advantage, and d) overall financial cost. It accounts for different return on investment and greater uncertainty in projected impact by not comparing vaccines against each other but instead providing a structured and consistent approach to considering each investment. As the economics of these vaccines will be preventing further spread, epidemics /pandemics and their additional costs, new and better economic measures are necessary. See Annex C to May 2023 PPC Doc 09 for details on the criteria and indicators.
- 3.8 The Gavi Board can review investment cases for epidemic diseases on an ad-hoc basis when necessary. In order to be prepared, the Secretariat works towards *living assessments* – a tool to monitor emerging data, highlight data gaps and facilitate timely decision-making between VIS cycles. These are updated on a regular basis as and when new evidence emerges and are developed for WHO's R&D Blueprint priority pathogens for which a vaccine in the R&D pipeline has obtained preliminary safety and immunogenicity data (Ph2a/b) and can also be triggered on an ad-hoc basis by a public health event (e.g. m-pox in 2022).⁷

4. Long-horizon market shaping

- 4.1 Market shaping activities at Gavi normally coincide with a Board decision to fund and begin the design of a vaccine programme. However, there is evidence that long-horizon or early market shaping can have a positive impact on

⁷ The Secretariat currently has living assessment for: chikungunya, Ebola, hepatitis E, hantavirus, Marburg, Rift Valley Fever, MERS, Nipah and m-pox. They can also inform the Global Virtual Pooled Inventory (GVPI) as proposed in Paper 09.

averting a market failure, preparing markets for optimised programme launches, and ensuring improved responsiveness and faster access to a vaccine in the event of an outbreak or epidemic, as evidenced by interventions for Ebola, Malaria or Hexavalent prior to a Gavi programme. Thus, as part of the VIS evaluation, the Secretariat in collaboration with partners, proposes to conduct a 'long-horizon market shaping assessment' for each vaccine on the VIS 2024 longlist with options and recommendations to be included as part of the VIS analyses and presented to the Steering Committee, PPC and Gavi Board as appropriate.

5. Exploring the potential value of supporting immunisation platforms for specific target populations

- 5.1 Gavi's primary focus has been and remains supporting infant vaccination, currently prioritising reaching zero-dose children and restoring and expanding routine immunisation services. In more recent years, through the introduction of HPV and a future DTP booster programme, Gavi is committed to strengthening vaccination platform to reach adolescents and this can be leveraged for future vaccinees in the R&D pipeline such as tuberculosis. In addition, Gavi now has experience supporting vaccines for other age groups (COVID-19, MCV2) as well as malaria.
- 5.2 Vaccines in the R&D pipeline are increasingly for non-infant target groups (dengue, group B streptococcus, tuberculosis). Considering this evolution and based on lessons learnt from reaching non-infant platforms, with the need to provide additional flexibilities (HPV), integration with other interventions (malaria) and additional support (COVID-19) to ensure sustainability and coverage beyond vaccine introduction, the Secretariat proposes to use the VIS 2024 as an opportunity to explore the potential value of providing support to develop, strengthen and deliver vaccines at new touchpoints for specific target populations. This approach would be an innovation to the VIS process that has traditionally focused on a vaccine per vaccine approach that served additions to the infant vaccination platform well. However, new immunisation touchpoints could benefit from a broader view of needs and support for vaccine delivery that could also pave the way for future vaccine introductions. Countries would decide which vaccines to deliver and Gavi support could address challenges in funding, implementation, and demand.
- 5.3 The Secretariat proposes to explore two additional immunisation touchpoints: **health worker** and **antenatal care**. A health worker⁸ touchpoint integrated into the existing health system protects health workers, ensures patient safety, builds resilient health systems, promotes uptake of vaccination in other target groups, enhances public trust in vaccination, and contributes to pandemic preparedness by establishing a mechanism for rapidly immunising health workers during future pandemics. This touchpoint builds on influenza work that

⁸ WHO defines health workers expansively as "all people engaged in work actions whose primary intent is to improve health" and recommends vaccination against eleven diseases (tuberculosis (BCG), hepatitis B, polio, diphtheria, pertussis, measles, rubella, Neisseria meningitis, influenza, varicella and COVID-19) for those not already immune. Influenza vaccine is recommended annually.

began under the Board's direction in 2005, and subsequently led to Board approval in 2018 of a learning agenda to assess the feasibility and impact of immunising health workers with seasonal influenza vaccines to support epidemic and pandemic influenza preparedness and which was completed in January 2023 (see details in Annex D to May 2023 PPC Doc 09).

- 5.4 An antenatal immunisation touchpoint would deliver vaccines to pregnant persons and newborns.⁹ This touchpoint integrated into the existing antenatal care system aligns with Gavi's focus on equity and social protection by protecting mothers, neonates and infants, and promotes coordination between EPI (Expanded Programme on Immunization) and MNCH (Maternal, Newborn and Child Health) services. Gavi support could address challenges in vaccine hesitancy and timing of visits and improve quality of antenatal care.
- 5.5 The VIS Steering Committee and PPC were supportive of the Secretariat exploring potential support to develop, strengthen and deliver vaccines at new touchpoints as part of the VIS. The PPC highlighted the opportunity of strengthening country systems through these touchpoints and the potential to reduce neonatal mortality through the antenatal touchpoint. The evaluation of these touchpoints will bring the necessary evidence to inform the development and review of Gavi's support for health systems as part of the strategy development for Gavi 6.0.

Section C: Actions requested of the Board

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

- a) **Approve** the longlist of pathogens (hepatitis E, m-pox, dengue, COVID-19, tuberculosis, group B streptococcus, chikungunya, and shigella) with licensed or pipeline products, to assess as new potential investments in vaccines and immunisation products through the VIS process;
- b) **Approve** the evaluation criteria for potential new investments in vaccines and other immunisation products primarily intended for ***endemic disease prevention***; these include key ranking criteria (health impact, value for money, equity and social protection, Gavi's comparative advantage and economic impact) and modulating criteria that inform the ranking (global health security impact, other impact, broader health system benefits, implementation feasibility, alternative interventions, and contribution to global agenda);
- c) **Note** the evaluation approach for potential new investments in vaccines and other immunisation products primarily intended for ***epidemic disease prevention***; centred around four key questions: i) disease burden and risk, ii) vaccine impact and feasibility, iii) fit for Gavi and partners, and iv) financial implications; and

⁹ For pregnant people WHO recommends tetanus-diphtheria-pertussis (Tdap), influenza, and COVID-19 vaccines, and when available, respiratory syncytial virus (RSV) and Group B streptococcus (GBS) vaccines. New-borns should receive BCG and hepatitis B.

- d) **Request** as part of the VIS, the Secretariat undertake further analyses to evaluate the potential value of providing support to develop, strengthen and deliver vaccines at new touchpoints for specific target populations building upon lessons learned from other Gavi programmes.

Additional information available on BoardEffect

Appendix 1 (in May 2023 PPC meeting book): Annex A to Doc 09 Vaccine Investment Strategy 2024: Longlist and evaluation frameworks – Implications/Anticipated impact

Appendix 2 (in May 2023 PPC meeting book): Annex B to Doc 09 Vaccine Investment Strategy 2024: Longlist and evaluation frameworks – Evaluation framework for endemic diseases: criteria and indicators

Appendix 3 (in May 2023 PPC meeting book): Annex C to Doc 09 Vaccine Investment Strategy 2024: Longlist and evaluation frameworks – Evaluation framework for epidemic diseases: criteria and indicators

Appendix 4 (in May 2023 PPC meeting book): Annex D to Doc 09 Vaccine Investment Strategy 2024: Longlist and evaluation frameworks – Background on seasonal influenza learning agenda

Appendix 5 (in PPC Library – Additional materials for May 2023 PPC meeting): Appendix 1 to Doc 09 - List of VIS Steering Committee members and summaries of meetings in December 2022 and April 2023 (draft), respectively.

Appendix 6 (in PPC Library – Additional materials for May 2023 PPC meeting): Appendix 2 to Doc 09 - Summary of results from country survey