

**SUBJECT:** GAVI'S ENGAGEMENT IN EBOLA VACCINE

**Agenda item:** 08

**Category:** For Decision

## **Section A: Executive Summary**

### **Context**

The current time-limited Ebola funding envelope approved in 2014 will come to an end in 2020; furthermore, since the Programme and Policy Committee (PPC) discussion in October 2019 the first Ebola vaccine was licensed and pre-qualified and licensed doses are expected to become available in mid-2020, with other vaccines to follow. Following discussion by the PPC, this paper proposes the opening of a new funding window for a long-term licensed Ebola vaccine programme. This would comprise support for reactive vaccination for outbreak response through an emergency stockpile – including vaccination in neighbouring countries – and preventive vaccination of high-risk groups outside of an outbreak (such as certain healthcare workers in countries classified as being at high risk).

### **Questions this paper addresses**

To consider the value of an Ebola vaccine programme this paper adapts the Vaccine Investment Strategy (VIS) evaluation approach for vaccines for epidemic preparedness and response approved in June 2018. This framework presents the four main questions:

- 1) Is the epidemic potential of Ebola Virus Disease sufficient to prioritise a stockpile? (Section 2)
- 2) Would use of the vaccine be feasible/impactful (and in what contexts)? (Sections 3,4)
- 3) What is Gavi's comparative advantage? (Section 5)
- 4) What are the financial implications? (Section 6)

### **Conclusions**

The Board is asked to approve the opening of a funding window for an Ebola vaccine programme with estimated financial implications of US\$ 9 million for 2020 and US\$ 169 million for 2021-2025. This funding window would replace the time-limited Ebola envelope approved in 2014. The Board is asked to approve retaining the health systems strengthening (HSS)/operational cost support window from the 2014 Ebola envelope in order to provide any required operational support for the use of investigational vaccine recommended by WHO, for the interim period before licensed vaccine doses are available in sufficient volume and the stockpile is operational including in the ongoing outbreak and other outbreaks that may occur.

The approach outlined seeks to enable the earliest possible procurement of licensed Ebola vaccine, whilst also ensuring flexibility based on: public health need; potential future availability of multiple vaccines with different use cases; and evolving SAGE (Strategic Advisory Group of Experts on Immunization) recommendations and vaccine demand.

## **Section B: Gavi's Engagement in Ebola Vaccine**

### **1. Gavi's engagement in Ebola to date**

- 1.1 In 2014, in the context of the West African Ebola outbreak, the Board endorsed up to US\$ 390 million for procurement and delivery of licensed Ebola vaccines and health systems recovery until 2020.<sup>1</sup> The decision included the use of Advance Purchase Commitments (APC) and in 2015 the Executive Committee approved an APC for future procurement of licensed vaccine with Merck, including a US\$ 5 million pre-payment on future licensed vaccine procurement. As part of the agreement, Gavi set three conditions including the submission of an application for licensure by a set date and the creation and maintenance of a stockpile of 300,000 doses of investigational vaccine (V920) to be made available and maintained for use in case of an outbreak through a donation to WHO. To date, more than 254,000 doses have been used, most recently in Eastern DRC (Democratic Republic of the Congo) and neighbouring countries. Gavi has also provided ~US\$ 16 million in funding to WHO to support vaccination costs in the Equateur and North Kivu outbreaks, and further funding was recently approved.<sup>2</sup>
- 1.2 As a result of this early engagement in Ebola vaccines, the Secretariat has been able to work closely with manufacturers, WHO and other partners to monitor developments relating to regulatory progress, supply and price, and communicate the Board's expectations of manufacturer transparency on cost of goods. The Secretariat has provided regular updates to the Board and in two instances the Market-Sensitive Decisions Committee has extended the deadline specified in the APC for submission of an application for licensure. These decisions were made acknowledging that the delays were driven by challenges faced in the development process, with consideration of the manufacturer's progress, and in recognition of the value of retaining the legal obligation by the manufacturer to maintain the investigational vaccine stockpile. Despite shifting timelines, the APC ultimately provided access to an investigational vaccine stockpile for use in outbreaks until vaccine licensure.

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<sup>1</sup> Of the US\$ 390 million, US\$ 100 million was committed from available Gavi funding and the remaining US\$ 290 million was to come from fundraising of new resources. Within the \$100 million, US\$ 70 was allocated for HSS & Operational Costs, of which US\$ 52.4 million remains for the period 2019-2020. Of the new resources to be raised, in 2017, USAID committed US\$ 20 million to fund a future Ebola stockpile with vaccines that have achieved all necessary regulatory approvals.

<sup>2</sup> An additional contribution of US\$ 13.4 million to WHO to support the DRC response has been approved and is pending disbursement.

- 1.3 Given that in 2020 the current Ebola envelope will end and the first licensed and prequalified Ebola vaccine doses will become available, the Board is requested to approve a new Ebola vaccine programme. This also takes into consideration the expectation that other vaccines will become available in the 2020-2025 timeframe.

## 2. Ebola Virus Disease

- 2.1 Historically the burden of Ebola Virus Disease (EVD) was characterised by small, infrequent outbreaks in several central African countries. However, two large outbreaks since 2014 have highlighted the potential for EVD to cause epidemics of unprecedented scale, spread and duration. To date, of the four Ebola species which cause disease in humans, most outbreaks have been caused by Ebola *Zaire*.
- 2.2 EVD causes severe disease in general, with the highest mortality in newborns and pregnant women. Healthcare workers (HCWs) are at high risk of infection (~20 times higher risk) due to exposure to cases in the context of their work.<sup>3</sup> Consequently, large outbreaks can devastate health systems, both from the direct impact of infection in the health workforce and the resulting disruption to other programmes such as routine immunisation and maternal, newborn and child health. Fear, stigma and disruption from an Ebola outbreak translates to a significant economic and social cost. The global response for the West African outbreak is estimated to have cost US\$ 5.9-8.9 billion<sup>4</sup> and studies reported disproportionate burden on girls/women in terms of access to health and education and labour force participation.<sup>5</sup>

## 3. Ebola vaccine pipeline

- 3.1 There are currently 5 Ebola vaccines in clinical development and 3 that have been licensed in their country of origin (2 in Russia and 1 in China) with different characteristics and expected availability (e.g. time to immunity; number of doses).<sup>6</sup> It is envisaged that these candidates could address either one or both of two potential vaccine use cases: (1) reactive and preventive vaccination in an outbreak setting, and (2) preventive vaccination in non-outbreak settings targeting high risk individuals.
- 3.2 The Merck V920 vaccine was licensed and prequalified in mid-November 2019.<sup>7</sup> Preliminary data from an observational study in the current outbreak

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<sup>3</sup> Selvaraj et al., "Infection Rates and Risk Factors for Infection Among Health Workers During Ebola and Marburg Virus Outbreaks."

<sup>4</sup> Office of the UN Special Envoy for Ebola (2015)

<sup>5</sup> Pregnant in the Time of Ebola: Women and Their Children in the 2013-2015 West African Epidemic.

<sup>6</sup> There are currently no candidate vaccines in the clinical evaluation phase with an indication for multiple strains of Ebola

<sup>7</sup> On 11 November, the European Commission granted a conditional marketing authorisation on recommendation of the European Medicines Agency and on 12 November, WHO prequalified the vaccine. Local registration in key countries (facilitated through the African Vaccine Regulators

reported efficacy of 97.5% when one dose was provided to individuals considered to be at high risk of EVD.<sup>8</sup> A second leading candidate is Janssen's vaccine regimen, which requires a dose of two different vaccines to be delivered 56 days apart. For Janssen's vaccine several studies have recently commenced or are planned in DRC, Guinea, Sierra Leone, Uganda and Rwanda and Janssen expects licensure based on animal rule from mid-2020. Refer to the WHO Overview on current Ebola vaccines for more information.<sup>9</sup>

#### 4. Ebola vaccine programme

4.1 In order to support comprehensive disease control and signal longer-term commitment to partners and stakeholders, the proposed Ebola programme includes support for two strategies: **vaccination for outbreak response through an emergency stockpile** (including preventive vaccination of HCWs/FLWs in affected areas and in neighbouring countries), and **preventive vaccination outside of an outbreak in high risk populations** (such as HCWs/FLWs). The latter depends on potential emerging evidence on duration of protection of one or more vaccines and SAGE recommendations. The Gavi-supported programme would be designed in consultation with partners and impact would be evaluated on an ongoing basis, with the intention of using learning to refine the programme. It is anticipated that the programme would evolve given future demand for vaccine, deployment experience, future availability of new vaccines and updated SAGE recommendations.

4.2 Each component of the comprehensive programme is further described below. Overall, the PPC was supportive of the recommendation to establish an Ebola vaccine programme and of the emphasis on likely evolution in the programme's early years and the importance of learning from experience.

##### 4.3 *Emergency stockpile for outbreak response*

4.4 Support for an emergency stockpile of Ebola vaccine(s) for outbreak response (used for both reactive vaccination and preventive/pre-emptive vaccination) would be informed by SAGE recommendations. SAGE currently recommends ring vaccination of contacts and contacts of contacts and vaccination of HCWs/FLWs (front line workers) in affected areas and neighbouring countries to respond to active outbreaks. Targeted geographic vaccination is an alternative approach where serious security, social or epidemiological challenges prevent implementation of ring vaccination. In April 2019, the SAGE Working Group on Ebola Vaccine and Vaccination gave guidance that a Gavi-funded stockpile for outbreak response should

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Forum [AVAREF]) is expected to follow shortly. The FDA has granted Merck V920 priority review with target action date set for no later than 14 March 2020.

<sup>8</sup> 95% confidence interval 95.8-98.5% and very low attack rates of Ebola (0.2 per 1000 vaccinees) when one dose is provided to individuals considered to be at high risk of EVD

<sup>9</sup> WHO R&D Blueprint: Overview of the current research, development and use of vaccines against Ebola (October 2019)

[https://www.who.int/immunization/sage/meetings/2019/october/CICG\\_sitting\\_plan.pdf?ua=1](https://www.who.int/immunization/sage/meetings/2019/october/CICG_sitting_plan.pdf?ua=1)

be maintained at 500,000 licensed doses of vaccine(s).<sup>10</sup> This was based on analysis conducted by the Alliance on historical epidemiology, demand scenarios, risk factors and public health goals.

- 4.5 The size of the stockpile will be revisited regularly based on experience from vaccine deployment, EVD outbreak epidemiology and updated SAGE recommendations. If global demand for vaccines increases in the coming years, due to new SAGE recommendations or expanded demand from countries, increased supply capacity and multiple manufacturers might be needed in the short- to medium-term to meet this demand and ensure vaccine security. WHO and the Gavi Secretariat are leading the development of a Global Ebola Vaccines Security Plan which will, in part, aim to address this issue.
- 4.6 *Stockpile management:* A coordinated mechanism will be established to operationalise the vaccine stockpile. It will draw from the International Coordinating Group (ICG) mechanism currently in place for other Gavi-supported stockpiles, but tailored to the specific needs of Ebola. The ICG<sup>11</sup> will be responsible for taking rapid decisions on allocation of stockpile vaccine, but given the need to ensure sufficient expertise regarding use of Ebola vaccine, additional stakeholders will likely need to be included. Other aspects of stockpile coordination and management will be led by Alliance partner organisations: WHO, UNICEF and Gavi Secretariat.<sup>12</sup> The PPC endorsed this approach and emphasised the need for coordination with other potential stockpiles (e.g. US and other country-specific stockpiles) to ensure efficient global allocation of vaccine.
- 4.7 *Policy considerations:* Access to Ebola vaccine from the stockpile would be provided in line with the 'principles for Gavi support for emergency vaccine stockpiles' approved by the Board in 2016.<sup>13</sup> However, given the expectation of resource-intensive delivery requirements (e.g. specialised cold chain; ring vaccination), operational support would be tailored to each country's context and consider complementarity with resources from other emergency response actors/mechanisms. The Secretariat will work with WHO and other partners to develop guidelines regarding the scope of support. The PPC recommended that Gavi take a structured approach to defining the scope of support for operational costs and ensure visibility and oversight through regular review.

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<sup>10</sup> April 2019 SAGE meeting;

[https://www.who.int/immunization/sage/meetings/2019/april/5\\_SAGE\\_April\\_2019\\_Ebola\\_Rees.pdf](https://www.who.int/immunization/sage/meetings/2019/april/5_SAGE_April_2019_Ebola_Rees.pdf)

<sup>11</sup> ICG member agencies currently include the International Federation of the Red Crescent and Red Cross Societies (IFRC), Medicines Sans Frontieres (MSF), UNICEF, WHO; the Gavi Secretariat participates as an observer.

<sup>12</sup> The Gavi Secretariat, WHO and UNICEF will be responsible for demand forecasting, stockpile sizing and related cost-effectiveness modelling, with UNICEF leading on procurement. The Secretariat will also work closely with UNICEF on market shaping and manufacturer engagement.

<sup>13</sup> Gavi-supported countries would access vaccine without a co-financing requirement. Non-Gavi supported countries or non-state actors would be able to access stockpile vaccine in emergencies (e.g. for imported cases) with a principle that they should reimburse the cost to Gavi afterward.

- 4.8 *Preventive vaccination in non-outbreak settings in high risk populations*
- 4.9 The target population and scope of countries supported for preventive vaccination would be based on future SAGE recommendations. As no recommendation has yet been provided, the Secretariat, in consultation with WHO, estimated the potential vaccine needs for financial forecast purposes only. A sub-set of 6-10 countries that could be considered to be at highest risk was identified, and it was assumed that the target population would be HCWs at highest risk of occupational exposure. In total, it is estimated that the programme would target ~25-40k HCWs.<sup>14</sup> Such a targeted approach is more likely to be cost-effective. Given that HCWs represent a new target group, there may be a number of programmatic and feasibility questions to be addressed in the initial years of programme roll-out. A mechanism to review and approve countries' requests for preventive vaccination in non-outbreak settings would need to be developed, which would closely link to the mechanism for allocation of stockpile vaccine for outbreak response. The PPC suggested the Global Task Force on Cholera Control as a potential model to consider.
- 4.10 *Policy considerations:* As for vaccination in an outbreak setting, tailored operational support would be provided given the new contact point and highly targeted strategy. Regarding vaccine funding, it is not recommended that co-financing be required. Given the anticipated size of this programme, a co-financing requirement would bring disproportionately high transaction costs and introduce risk that a co-financing default for an Ebola programme could jeopardise routine vaccine programmes. It could also create barriers to vaccination of this target population, which is intended to protect broader health systems. The PPC agreed with this approach but asked the Secretariat to provide a review of this approach two years after the start of the programme. The PPC also clarified that this approach should not be assumed for future Gavi-supported vaccines for epidemic diseases.

## 5. Fit for the Alliance and strategic considerations

- 5.1 This request builds on the 2014 approval of Gavi's engagement in Ebola and the case for a role for Gavi remains strong. Gavi-supported countries face greatest threat of Ebola outbreaks and are disproportionately affected when they occur. A Gavi-supported programme would enable countries to plan for use of vaccines as part of their preparedness and risk mitigation activities, thereby limiting the broader impact on health systems (including routine immunisation). Gavi's commitment to Ebola vaccine procurement would also support market shaping objectives and incentivise development of second-generation vaccines. In addition, continued engagement would be aligned with the Gavi 5.0 objective of enhancing outbreak response through availability and strategic allocation of vaccine stockpiles.
- 5.2 *Risk of inaction:* If Gavi were not to engage it is unlikely that another global mechanism would fund an Ebola vaccine programme and Gavi-supported

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<sup>14</sup> Defined as HCWs likely to work in an Ebola treatment unit (ETU), members of a standing national response team (where established) and a subset of laboratory workers (~10% of HCW population)

countries, including those that participated in trials to generate evidence, would not have a mechanism to access vaccine. The negative signal could also undermine investment in new vaccines for Ebola, as well as other diseases which also have unpredictable need and limited markets. In addition, large and protracted Ebola outbreaks have a negative impact on access and coverage to other Gavi-supported vaccines thereby affecting broader immunisation goals.

- 5.3 Looking ahead, there are several strategic issues which Gavi will need to explore together with other stakeholders as we learn from initial experiences. For example incentives for development of second-generation (e.g. multi-strain) vaccines, sustainable manufacturing approaches and approaches to monitoring, evaluation and impact. Some of these questions will have broader relevance for other outbreak vaccines.

## 6. Financial implications

- 6.1 The forecasted financial implications are US\$ 9 million for 2020 and US\$ 169 million for 2021-2025. This is comprised of vaccine procurement costs of ~US\$ 8 million for 2020 and ~US\$ 133 million for 2021- 2025; operational cost support of ~US\$ 32 million for 2021-2025; and Secretariat and Alliance partner costs of ~US\$ 1 million for 2020 and ~US\$ 4 million for 2021-2025.<sup>15</sup> A large proportion of the projected financial implications are associated with the establishment and operation of the Ebola emergency stockpile. The financial forecast assumptions include possible procurement of multiple vaccines within the stockpile. The 2021-2025 costs are in line with the projection of Ebola expenditure that was included in Gavi's 2021- 2025 investment opportunity (US\$ 150 million).
- 6.2 In the interim period before licensed vaccine is available in sufficient volume and the stockpile is fully operational, the 2014 Ebola envelope will be used for the HSS/operational cost support window (of which US\$ 52.4 million remains) to provide operational support for use of investigational vaccine recommended by WHO, including in the ongoing DRC outbreak or in the event of another Ebola outbreak before a licensed vaccine is available (projected mid-2020).<sup>16</sup>
- 6.3 The market for Ebola vaccines will be limited in the short/medium-term to a stockpile procured by the US government and the Gavi-funded stockpile, although in the longer-term other governments or organisations may also wish to procure Ebola vaccines. This is likely to result in comparatively high vaccine prices, as the relatively low global demand compared to other vaccines will mean that costs are not offset by procurement of high volumes, as is the case for other Gavi-supported vaccines. Additionally, vaccine prices are expected to be higher in the first years of procurement as production is scaled up. Over time, and as new vaccines come to market,

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<sup>15</sup> Gavi will seek to absorb the Secretariat and PEF-related components in the 2020 estimated costs within the 2020 budget submission

<sup>16</sup> The additional contribution of US\$ 13.4 million to WHO to support the DRC response has been approved and is pending disbursement.

there may be increased synergy and cost reduction. The projected financial implications and key underlying assumptions (e.g. stockpile size) would be reviewed and revised regularly. In the event of materially increased demand for Ebola vaccine or that future SAGE recommendations imply that a significant increase in financial resources would be required to support the Ebola programme, the Gavi Secretariat would return to the Board with a revised request.

### **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 opening of a funding window for the establishment of an Ebola programme for licensed vaccines used for i) reactive and preventive vaccination in an outbreak setting through an emergency stockpile and ii) preventive vaccination in a non-outbreak setting, ~~both~~<sup>17</sup> contingent on WHO prequalification of vaccine and SAGE recommendation, in line with Board-approved policies and decisions with adjustments laid out under b), c) and d);
- b) **Approve** Gavi support for vaccines for preventive use without a co-financing obligation for Gavi eligible countries with the co-financing policy for Ebola vaccine subject to review after two years from start of programme;
- c) **Approve** Gavi operational cost support for both reactive and preventive vaccination that is tailored to each country based on context;
- d) **Approve** the principle of providing non-Gavi eligible countries access to vaccines for preventive vaccination, where possible. These countries would bear the cost of the vaccine;
- e) **Note** the financial implications associated with the above approvals for vaccine procurement, operational cost support and Secretariat and partner resources for 2020 is expected to be approximately US\$ 9 million and for 2021-2025 is expected to be approximately US\$ 169 million. Gavi will seek to absorb the Secretariat and PEF-related components in the 2020 estimated costs within the 2020 budget submission;
- f) **Note** that the Secretariat will work with partners to further develop processes to enable allocation of vaccines and operational cost support for both reactive and preventive use;
- g) **Approve** retaining the operational cost and health system support component of the 2014 Ebola envelope for the interim period before a licensed vaccine is available in order to provide operational support for use of investigational vaccines and closing the remainder of the 2014 Ebola envelope; and

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<sup>17</sup> This edit to the decision point reflects the recent licensure and prequalification of the Merck Ebola vaccine in November 2019, subsequent to the PPC meeting in October 2019.



- h) **Note** the remaining balance of the operational cost and health systems support component of the 2014 Ebola envelope of US\$ 52.4 million.

**Annexes**

**Annex A:** Implications/Anticipated impact

**Additional information available on BoardEffect**

**Appendix 1 (in October 2019 PPC meeting book):** Doc 08 *Gavi's Engagement in Ebola Vaccine*