Subject	**Human papillomavirus (HPV) Vaccine Programme relaunch**
Agenda item	**07**
Category	**For Decision**

Section A: Executive Summary

Cervical cancer is 70-90% preventable through Human Papillomavirus (HPV) vaccination, yet 342,000 deaths were recorded in 2020, with ~90% of these occurring in low- and middle-income countries (LMICs). HPV vaccine has amongst the **highest impact**[1] and is the key intervention towards the ambitious WHO 2030 targets to achieve cervical cancer elimination[2].

In 2021, global HPV coverage stood at 12%, while 9% in Gavi73 and 4% in eligible Middle-Income Countries (MICs) [3]. Severe supply constraints have been the major driver behind low coverage in LMICs and impeded progress during Gavi 4.0 (2016-2020)[4]. Other drivers include vaccine/operational costs; competing priorities; the unique challenges of vaccinating adolescent girls (such as service delivery, gender-related barriers, demand and trust, lack of existing touchpoints within the health system); and COVID-19 pandemic disruptions including school closures.

HPV vaccination is critical to **reduce cervical cancer**, especially in lower-income countries with high disease burden and weak secondary prevention programmes. It is also a bridge to women and girls' health and an opportunity to positively impact gender equity. The new WHO SAGE (Strategic Advisory Group of Experts on Immunization) recommendation permitting countries to opt for a single-dose schedule and an increased global supply provides a **critical opportunity to inject renewed momentum**. To accelerate the number of girls reached with HPV, from 9.8 million (2021) to the ambitious target of ≈86 million by 2025, the following objectives have been set: 1) accelerate quality introductions; 2) rapidly improve global and national coverage; and 3) generate long term programmatic sustainability through building and integrating HPV vaccination within routine delivery mechanisms and into Primary Health Care (PHC).

[1] Vaccine Impact Modelling Consortium (VIMC), 2022
[2] To achieve this, 90% of girls should be fully vaccinated with HPV vaccine by 15 years of age; 70% of women should be screened using a high-performance test by age 35, and again by age 45; 90% of those identified with cervical disease should receive appropriate treatment.
[3] MICs-eligible countries refer to the 45 countries and economies that are eligible under the MICs Approach: all former-Gavi, never-Gavi lower middle-income countries (LMICs) and never-Gavi-International Development Association (IDA)- eligible economies). Uzbekistan/Nicaragua, whilst now eligible for the MICs Approach, are reported as Gavi 57.
[4] Original 2020 target was 40 million girls, only reached 7.1 million girls by end of 2020 (Gavi APR 2020)

Section B: Context

1. HPV vaccine programme: Context, status, learnings (see Appendix 1 for detailed background)

1.1 To date, Gavi has successfully supported 27 countries to introduce the HPV vaccine into national immunisation schedules reaching 9.8 million girls[5]. ~90%[6] of countries globally that have not yet introduced are Lower Middle-Income Countries (LMICs), including populous countries. In addition, since the onset of the COVID-19 pandemic, global coverage for Gavi73 HPV vaccination rates was reported in 2021 at 11% HPV1 and 9% HPV2[7] showing a downward trend.

1.2 Aside from COVID-19, vaccine supply shortages have also impacted Gavi's HPV target[4]. Severe supply constraints (2017-2021[8]) resulted in 12 countries[9] that are yet to conduct their Multi Age Cohort (MAC) catch-up (i.e. reaching girls 10-14 years outside the routine single aged cohort of 9 years), representing approximately ~22 million girls pending vaccination. However, the current supply outlook is favourable, with total supply availability (from historical manufacturers/new entrants) expected to triple between 2022-2025.

1.3 Though Gavi prices range from as low as US$ 2.90 to US$ 5.18/dose, vaccine costs are frequently cited as a barrier. For never Gavi-eligible LMICs and International Development Association (IDA)-eligible economies this is even more of a challenge with prices quoted for procurement ranging from US$ 10.25 to US$ 31.50/dose. The June 2022 Gavi Alliance Board-approved 'Middle-Income Countries approach' and the proposed extension of accelerated transition status under the Funding Policy Review (Doc 10) aims to address these access and sustainability issues.

1.4 To date, lessons learned in immunisation for school-aged contact points and adolescents have shown: the importance of **strengthening the enabling environment** (i.e. policies, multi-sectoral coordination, data and information systems); the need to **optimise and diversify pro-equity delivery channels** (e.g. linkages to and with schools, communities and health facilities) per country context to identify high coverage and sustainable models and; **community-based and tailored demand generation** to address socio-cultural barriers through promoting gender-responsive approaches that could impact future

[5] Gavi Annual Progress Report 2021
[6] ~65% Low-income countries (LICs)/Lower middle-income countries (LMICs), ~25% Upper middle-income countries (MICs)
[7] WHO refers to HPVc- completed schedule for historical reasons as some countries were on 2 and 3 doses and some are still on this schedule. However, given that all Gavi73 are on 2-dose schedule we refer to HPV2
[8] The projected demand for 2020-2021 was estimated at 59.5 million doses, however only 29 million doses were supplied, resulting in a shortfall of 30.5 million doses
[9] Burkina Faso, Cameroon, Cote d'Ivoire, Ethiopia, Kenya, Malawi, Mozambique, Myanmar, Liberia, Senegal, Tanzania, Zambia

generations. In parallel, implementation research is required to support **iterative investments for high impact HPV programme models** (e.g. reaching vulnerable populations, including out-of-school, HIV+ populations, integrated package of care).

1.5 In November 2022, the Secretariat presented to the Programme and Policy Committee (PPC) a proposed relaunch for the HPV programme (see Appendix 1) which seeks to address the afore mentioned challenges and opportunities (see Annex A). The **PPC unanimously expressed support for the relaunch in view of the high impact of HPV vaccination.** The PPC emphasised the need for timely operationalisation of the proposed funding approach reiterating the need for flexibility and speed to achieve the ambitious targets. The Secretariat has initiated a review and planning for operationalisation of these funds while ensuring synergies and streamlining across existing Gavi funding levers. As per a request from the PPC, the Secretariat has committed to updating the PPC twice annually on implementation progress and shall return to the Board should further funding or flexibilities be needed.

2. Proposed strategic shifts to Gavi's HPV programme and potential impact

2.1 To achieve the following three objectives 1) accelerate quality introductions; 2) rapidly improve global and national coverage; and 3) generate long term programmatic sustainability through building and integrating HPV vaccination within routine delivery mechanisms and into Primary Health Care (PHC), **four strategic shifts** are being proposed. To help the Alliance achieve its ambition[10] the Secretariat with Alliance partners shall: 1) update HPV vaccine programme guidelines to facilitate and accelerate adoption of permissive 1-dose schedule; 2) optimise and increase the relevant HSS investments/mechanisms that support accelerating and strengthening of the HPV programme (i.e. school age / adolescent touch points); 3) enhance technical assistance through Partners' Engagement Framework (PEF) Targeted Country Assistance (TCA) and Foundational Support (FS); and 4) establish learning agenda support through the PEF Strategic Focus Area (SFA) for integration of the HPV vaccination programme in routine immunisation delivery mechanisms and Primary Health Care (PHC).

2.2 While the Gavi Secretariat and Alliance partners recognise the unpredictability of countries fully embracing and integrating the strategic shifts, given the high impact of HPV vaccination, we propose to **maintain an ambitious target of reaching >86 million girls by 2025 averting over 1.4 million future deaths[1] from cervical cancer (see Annex B)**. Considering both Gavi and country funding, this translates in a cost per death averted of US$ 430. To achieve this, routine HPV coverage would increase to 39% across the Gavi57 countries. Given current routine HPV coverage is 9% in Gavi57 countries, reaching 39%

[10] These proposals relate to support for Gavi-eligible countries. MICs-eligible countries are supported with the introduction of HPV through the MICs Approach.

by 2025 will require substantial investment in the relaunched HPV programme, full and rapid absorption, and quality implementation by country EPI programmes.

2.3 *Strategic shift 1: update HPV vaccine programme guidelines to facilitate and accelerate adoption of permissive 1-dose schedule:* Gavi's programme funding guidelines for routine and multi-age cohort (MAC) will be updated as per the recent SAGE meeting (April 2022) and the anticipated WHO paper on recommendation for a permissive single dose HPV vaccination schedule[11]. This creates an opportunity for increased uptake and coverage, eased supply pressure, reduced vaccine costs and programme implementation costs, more programme flexibility, and increased financial sustainability of HPV vaccine delivery. The updated guidelines **encourage adoption of a single dose schedule, noting that the final decision between a permissive 1-dose or 2-dose vaccination schedule rests with the country**. Countries with 'delayed' MACs, particularly those with coverage <50%, provide a unique opportunity to re-accelerate the HPV programme and rapidly restore coverage by catching up girls who missed their vaccination. Additional vaccine cost per the relaunch is estimated at US$ 69 million and cash support (Vaccine Introduction Grants - VIGs/Ops) at US$ 9 million (see Annex C).

2.4 *Strategic shift 2: Optimise and increase the relevant HSS investments/mechanisms that support accelerating and strengthening of the HPV programme:* In general, health systems in Gavi-supported countries have limited touch points with adolescents, few well-developed school health programmes and adolescent girls can experience significant gender-related barriers accessing health services. As such, many countries will need to strengthen the capacity of their health systems to be responsive to adolescent needs. To address this the Alliance proposes to bring a more deliberate focus on scaling up HPV vaccination within its HSS grants, complementing VIGs and operational cost grants. The objective would be to **strengthen health systems' capacities to reach adolescents** and learn what it will take for countries to build an effective adolescent immunisation programme in consideration of a potential life course approach to immunisation in Gavi 6.0. This will help to address budget gaps at introduction (e.g. demand, service delivery) and support long-term investments for normalisation and routinisation of HPV into routine immunisation delivery mechanisms and PHC (e.g. demand generation, data, human resources, school-based delivery, other multi-sectoral partnerships). Dedicated HPV investment in HSS is estimated at US$ 40 million and the Secretariat shall return to the Board should further funding be needed.

[11] The data reviewed shows one dose provides comparable levels of individual protection and would be more cost-effective and efficient (fewer doses per cancer case prevented). Applies to those HPV vaccines for which corresponding 1-dose data have been collected — bivalent (Cervarix®), quadrivalent (Gardasil®), and nonvalent (Gardasil® 9) vaccines, new entrants single dose data expected 2024-2027

2.5 *Strategic shift 3: Enhanced technical assistance through Partners Engagement Framework (PEF) Targeted Country Assistance (TCA) and Foundational Support (FS):* There is a need to continue the introduction agenda (large country introductions, single dose adoption, MACs), and to support countries to address gaps in HPV programme performance. To do so, the Alliance will require dedicated funding for technical assistance for HPV within the PEF (TCA (US$ 28 million), and FS (US$ 2 million) buckets). We propose to use these resources to **complement, reinforce, expand and revitalise the current TA model at global, country, and sub-national levels through 4 priorities**: 1) continue accelerating country-level HPV decision making and introductions; 2) reinforce national and sub-national planning, coordination and implementation; 3) leverage opportunities for multi-sectoral programming; and 4) advocacy for HPV vaccination and adolescent health. Technical assistance funding will be allocated to countries on a need basis, and it will be communicated and monitored through the established PEF mechanisms.

2.6 *Strategic shift 4: Learning agenda support through PEF Strategic Focus Area (SFA) for integration of the HPV vaccination programme in routine immunisation delivery mechanisms and Primary Health Care (PHC):* HPV vaccination is often cited as an opportunity for immunisation and the broader health sector to connect with adolescents, and for secondary cervical cancer prevention interventions. However, there is limited experience of implementing HPV vaccination within routine immunisation or with other adolescent health interventions, for example, limited understanding of optimal delivery models. Lessons learned from e.g. Tanzania, Togo, show that operational details are key to success or failure. For these reasons, the Secretariat propose an **operational research agenda** to gather evidence for future implementation and policies on integrating HPV into routine immunisation delivery mechanisms and PHC and capture data on integrated interventions, logistical feasibility, and costs. Country prioritisation will be intentional so that the proposed research agenda also captures HPV learnings on reaching specific groups like girls out of school, HIV+ populations, delivery in fragile settings, and addressing gender-related barriers. This operational research conducted across a diverse group of countries will also carry important learnings for HPV introduction in fragile and conflict settings. This SFA funding is estimated at US$ 15 million.

3. Summary of financial needs for HPV relaunch 2023-2025

3.1 The initial proposed funding related to the HPV relaunch is included within the updated financial forecast at an estimated cost of US$ 167 million[12] resulting in total forecast expenditure of US$ 611 million for the HPV vaccine programme, as presented to the Board for approval. Of the relaunch funds, US$ 40 million sits in HSS; US$ 45 million in PEF envelopes with US$ 78 million in the vaccine budget line (both vaccines and cash support). Further details are in Annex C.

[12] See Board Agenda Item 4a, Financial Update, including forecast

Should the programme require additional funding, we will return to the PPC and Board. Should we face an urgent need before these timelines, existing flexibility granted to the CEO can be used.

Section C: Actions required of the Board

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

a) **Approve** the four strategic shifts for the HPV programme relaunch, which are:

1. To facilitate and accelerate adoption of a permissive 1-dose schedule and support recovery of original and missed cohorts up to 18 years of age for countries with delayed multi-age cohort (MAC) vaccinations;
2. Optimise and increase the relevant HSS investments/mechanisms that support accelerating and strengthening of the HPV programme;
3. Enhanced technical assistance through Technical Country Assistance (TCA) and Foundational Support (FS);
4. Learning agenda support through Strategic Focus Area (SFA) for integration of the HPV vaccination programme in routine immunisation delivery mechanisms and Primary Health Care (PHC).

b) **Note** that the HPV vaccine has amongst the highest impact of all Gavi-supported vaccines and **request** that the Secretariat update the Programme and Policy Committee twice annually on implementation progress and return to the Board should further funding or flexibilities be needed to deliver on the ambitious relaunch agenda.

Annexes

Annex A: HPV programme relaunch risks and implications

Annex B: HPV volume forecast scenarios

Annex C: Financials for HPV programme relaunch 2023-2025

Additional information available on BoardEffect

Appendix 1 (in October 2022 PPC meeting book): Doc 06: *HPV vaccine programme relaunch*