Annex A: **HPV programme relaunch risks and implications**

Secretariat risks/implications:

- **HR:** anticipated workload for the HPV programme relaunch will substantially increase per the proposed ambition and necessary shifts, therefore budget includes support for Secretariat and Alliance partners (for breakdown of budget please see Annex F).
- **Operational:** to facilitate iterative and adaptive implementation, grant processes will need to be reviewed and adapted with lens of simplicity, flexibility, and agility to allow for rapid disbursement, timely course correction and iterative implementation, and therefore accompanied by real-time monitoring and clear indicators, including lessons learned, to measure and evaluate impact and inform future investments in Gavi 6.0.
- **Reputational:** if there is slow HPV uptake including due to operational complexities and fund availability, the Alliance will not reach its proposed ambition of 86 million girls. To mitigate this, there will be close financial tracking and review of existing processes to identify, escalate and resolve bottlenecks that may arise.

Country risks/implications:

- **Country bandwidth:** countries have an increasing workload beyond their routine programmes, including COVID-19, new vaccine introductions such as malaria, outbreak response, and zero-dose agenda that could compromise focus on HPV vaccination. To mitigate this risk the proposal includes consultations with countries and HPV TCA funding to country, including support to EPI for dedicated country coordinators (e.g., per experience for Sierra Leone's introduction) and allocation framework which will account for programmatic readiness and competing priorities before moving countries forwards. In the case of former Gavi-eligible countries, dedicated support for new vaccine introductions – including country-specific technical assistance – is available through the MICs Approach.
- **Decision-making:** Lack of a regulatory pathway to achieve licensure for 1-dose may create inconsistency between PQ status and country decision for 1-dose therefore challenges may occur on the decision-making pathway for 1-dose (e.g. National Regularity Authorities, National Immunisation Technical Advisory Groups). This will be addressed through PEF including TCA (e.g. development of normative guidance, simulation models on the long-term benefit / risk and costs implications of adopting single-dose, facilitation of NITAGs), leveraging existing funded HPV technical bodies (e.g. HPV Vaccine Acceleration Program Partners Initiative (HAPPI) Consortium Single-Dose HPV Vaccine Evaluation Consortium, the Coalition to Strengthen the HPV Immunization Community (CHIC), Choice Optimization for Immunization: Country Exercises in Sustainability (CHOICES) projects) and WHO/UNICEF to advise manufacturers and countries to navigate the regulatory implications that could arise due to the inconsistency in labelling (e.g. leverage lessons learned from off-label IPV fractional doses recommendation).

Again, in the case of former Gavi-eligible countries, dedicated support for new vaccine introductions is available through the MICs Approach.

- **Programme complexity:** if country decides to stay on routine 2-dose but implement MAC as 1-dose, Gavi will require countries to provide strong justification. If durability of protection of single dose is shown to wane, Gavi will commit to supporting countries to switch back to a 2-dose schedule through available switch grant. Potential complexities of different schedules between populations (i.e. non-HIV+ vs HIV+), TA to support countries with normative guidance (i.e. required communications/training).

Alliance risks/implications:

- **Partner bandwidth:** current partners are supporting multiple agendas (e.g. COVID-19, other vaccine introductions including malaria, response to outbreaks), therefore PEF TA to provide resources to complement, including partners with new expertise in adolescent health and dedicated global/country coordinators. The Secretariat proposes to integrate the financial needs for HPV TA into the PEF and believe it can be absorbed for the most part within the existing envelope given historical and actual underutilisation in PEF SFA and TCA. However, if HPV needs turn out to be higher than expected or there is higher than expected utilisation of PEF for other activities, there is a risk the funding may be insufficient. We will monitor this closely and bring back to the Board if this unfolds in accordance with the standard financial forecast process to revise cost estimates (value & phasing) for Board approved programmes. Note that in the case that partner support is required for former Gavi countries, this can be provided through the MICs Approach.

Market shaping risks/implications:

- **Demand for new entrants:** Currently, the 1-dose schedule recommendation applies to the two “original” vaccines (from GSK and Merck). New and future entrants are in the process of planning for 1-dose schedule trials, and we expect them to seek 1-dose approval between 2024-2027. In the interim, an accelerated adoption of 1-dose schedule may put market health at risk, with high reliance on historical manufacturers and limited competition. Direct engagement and support to country decision making and development of a closely monitored allocation framework will support mitigation of this risk.

- **Supply necessary to achieve ambition:** The HPV programme relaunch has been designed with a clear view on available supply through Gavi 5.1, although unexpected production issues are a constant background risk in vaccine markets. Looking ahead to enhancing HPV market health (and hence reducing supply security risk, among other objectives), the Alliance Market Shaping Roadmap for HPV vaccines is being updated and is expected to be finalized in 2023. Strategy development will be based on analysis of the market and expected future supply and demand scenarios, accounting for product preferences of current and expected future product profiles, as well as any additional demand that may be generated through the MICs Approach. Some of the key questions that Roadmap

Partners will address include impact of 1-dose (as mentioned above) and expected country product preferences; how to ensure balanced demand across products, supplier sustainability and long-term competition in a 1 dose schedule environment; and how to ensure a healthy market transition to HPV9. The roadmap will also be aligned with the updated Allocation framework to adhere to the principles articulated while also ensuring and improving market health.

Financial risks/implications:

- **Lack of timely and sufficient HSS funds:** The Secretariat is seeking to integrate HPV relaunch financial needs into the HSS envelope to ensure synergies with other routine immunisation strengthening activities and believe this can be absorbed within the existing envelope. The Secretariat has initiated mapping and prioritizing which countries are likely to require additional HSS funding and putting in place agile processes to ensure money can be made available rapidly including, for example, rapidly approving reallocation of existing HSS in-country balances. If HPV needs turn out to be higher than expected or there is higher than expected utilisation of HSS for other activities, there is a risk the funding may be insufficient. We will monitor this closely and bring back to the Board if this unfolds.