Annex B: Human Papillomavirus (HPV) revitalisation update

Section 1: Executive Summary

As HPV revitalisation remains a Must Win priority during Gavi 5.1, the Board has requested bi-annual updates on progress. This annex updates on progress made between May and October 2024, highlighting HPV scorecard performance, WHO coverage estimates, and updates on implementation of the strategic shifts supporting the revitalisation goal.

The ambitious aim of immunising 86 million girls by the end of 2025 remains on track. In 2023, over 14 million girls were vaccinated with Gavi's support, compared to 13.3 million in the last decade bring the total number of fully immunised girls to 27.3 million since 2014, averting over 605,000 future cervical cancer deaths. HPV vaccine coverage in Gavi-supported countries doubled from 8% in 2022 to 16% in 2023.16 routine programs and 14 multi-age cohort (MAC) campaigns have launched as part of Gavi 5.1, with new introductions in large countries like Nigeria and Bangladesh. Fourteen countries have transitioned from a two-dose to a single-dose schedule. Five additional countries have had their applications for HPV support approved since May 2024.

Establishment of 19 Partner Framework Agreements to facilitate rapid and fit-for-purpose Targeted Country Assistance and the launch of seven integration learning projects are recent successes that will bolster HPV revitalisation through 5.1 and into 6.0. To meet the 86 million target by 2025, continued focus is required on improving coverage, launching large campaigns, and ensuring timely vaccine supply.

Section 2: Programme Status

The HPV vaccine programme has made significant progress in achieving the strategy's objectives: i) accelerate quality introductions; ii) rapidly improve global and national coverage; and iii) generate long-term programmatic sustainability by integrating HPV vaccination into routine delivery mechanisms and Primary Health Care (PHC).

2.1. Update to the HPV Scorecard

Under the HPV measurement framework, the scorecard is used to monitor progress at Impact, Outcome, and Output level. Current status shows that all indicators are on track to be achieved by the end of 2025, but with a risk to achievement of the overall indicator for number of launches and VIG/Ops disbursement. Further details follow in the referenced sections of this Annex.

Figure 1: Performance against HPV Scorecard Indicators in Gavi 5.1

Performance against HPV Scorecard indicators in Gavi 5.1

		Cumulative to 2022	Cumulative to 2023	Cumulative to 30 Sep '24	Status	Target (2025)	Relevant annex section
Impact	Cervical cancer deaths averted (from 2014)	>330k	>605k	*		1.4m	2.2
Outcomes	New HPV launches (from 2021)	8R, 7M	14R, 12M[1]	16R, 14M		27R, 28M	3.1
	HPVC coverage in Gavi57 (annual figures)	8%	16%	*		21% (+17pp[2])	2.2
	Girls fully immunized (from 2014)	>13.3m	>27.3m	*		86m	2.2
						Milestone (2024)	
Outputs	HPV applications approved by IRC (from 2021)[3]	4	8	18		16	3.1
	% HPV VIG/Ops disbursed (from 2021)[4]	6%	40%	56%		74%	3.1
	Number of HPV countries with TCA contracted[5]	NA	30	33		34	3.2–3.3
	Number of countries supporting HPV with HSS[6,7]	3	7	14		14	3.4

NA, not applicable. R routine, M multi-age cohort (MAC).
[1] Updated in August 2024 to include a self-financed MAC in Eswatini. The HPV programme in Eswatini is supported by MICs TA.
[2] Relative to 2019 coverage baseline
[3] Excludes applications that may be approved through alternative review mechanisms.
[4] Cumulative disbursed for VIG/Ops vs Gavi 5.0/5.1 forecast. Future disbursements may change due to updates to 5.0/5.1 forecast. In December 2022 the Board approved an additional US$10m for VIG+Ops+switch, hence the lower cumulative disbursements against 5.0/5.1 totals in 2021 and 2022.
[5] Countries start to be included in the total when funds are contracted. Includes activities that are funded through either TCA ceilings or the TCA reserve.
[6] New or reprogrammed HSS funding for HPV per the December 2022 Board decision on the HPV relaunch. Note that three of these countries drew on HSS explicitly for HPV in 2022 (Kenya, Sierra Leone, and Lao PDR), for activities to occur in 2023.
[7] Currently on track relative to target. HPV working group and HSIS team are closely monitoring and addressing risk of delays emerging where interest in HSS funding has been slow to materialize into applications.

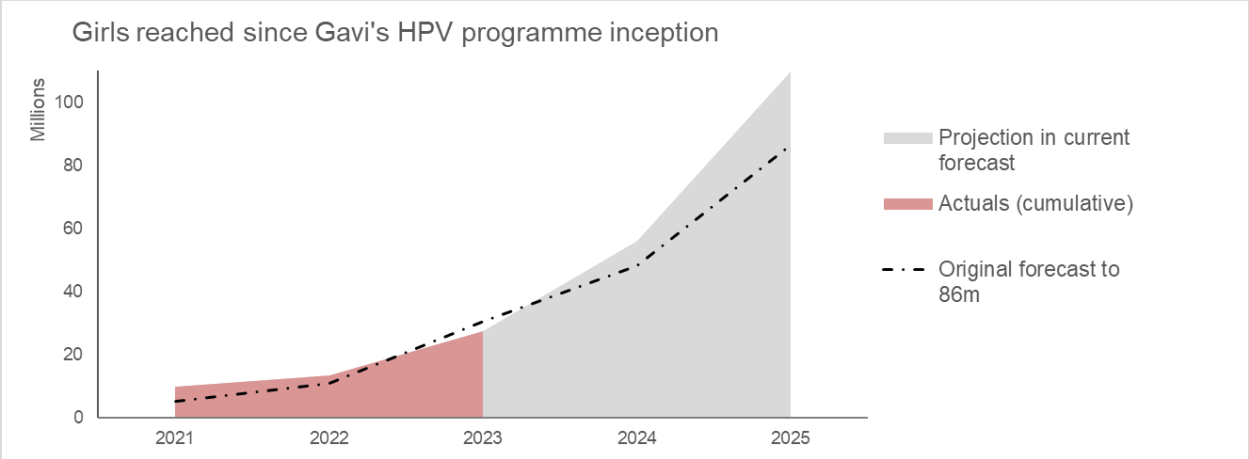
On track · Moderate delays / challenges · Significant delays / challenges · No update

2.2. World Health Organization (WHO) Coverage Estimates Updates

New WHO coverage estimates for the last dose in the schedule for HPV vaccine (HPVC) indicate that more girls were reached in 2023 (14 million with Gavi support) than the prior 10 years of the programme (13.3 million with Gavi support), bringing the number of girls fully immunised since 2014 to 27.3 million. These figures translate to >605,000 future cervical cancer deaths averted with Gavi support. HPVC coverage in Gavi57 countries was 16% in 2023, rising from 8% in 2022, and first dose coverage (HPV1) reached 20% in 2023, up from 12% in 2022. Increases were driven by new introductions in large countries including Bangladesh and Nigeria, and by coverage improvement in existing programmes including through catch up activities and switches to a single dose schedule. It should be noted that the WHO estimation process attempts to make the best use of all available data, and this year new coverage surveys were incorporated into the WHO estimates in triangulation with administrative data. This newly available survey data led to a downwards revision in historical coverage estimates for Ethiopia.

The updated Gavi Secretariat vaccine forecast (v22) indicates the programme is largely on track to reach 86 million girls by the end of 2025. Meeting this ambitious aim will depend upon sustaining and improving coverage in existing programmes and launches of large campaigns and introductions before the end of 2025, including a delayed multi-age cohort (MAC) campaign in Ethiopia, and introductions in India and Pakistan.

Figure 2: Projection of girls reached with HPV vaccine by end of Gavi 5.1



In December 2022, the Board approved the recovery of original and missed cohorts for countries with delayed multi-age cohorts. There are two countries – Cameroon and Myanmar – that have a preference to conduct their MACs in 2026, and have not yet secured HPV doses for MAC launch in 2025. The Secretariat has reflected these two delayed MACs in 2026 in the v22 forecast, so that they can be implemented in 2026, contingent on availability of funding during Gavi 6.0.

Section 3: HPV Programme Update

3.1. Vaccine Introductions

Since the last update to the Board in June 2024, Timor-Leste introduced the HPV vaccine in July 2024 under Post-Transition Engagement support. Timor-Leste's programme launched with a self-financed MAC campaign to target girls up to age 14. In May 2024 the second and final phase of Nigeria's HPV vaccine introduction launched following the first phase in October 2023. Phase 2 reached more than 7.3 million 9-14 year old girls in 21 states. This brings the total HPV vaccine launches to 16 routine programmes and 14 MACs in Gavi 5.1 to end September 2024.

The ambitious target to support 27 routine launches and 28 MACs between 2021-2025 remains within reach, however is conditional upon timely vaccine supply and preparedness activities in 2024 and 2025. Since May 2024, five applications for HPV support have been recommended for approval by the Independent Review Committee (IRC), including applications from Ghana, Comoros, and Pakistan, and applications for MICs support from Tunisia and Cuba. In addition, two countries have been approved to launch delayed MACs in 2025 through the internal Secretariat review process since May 2024 – Malawi and Liberia. All told, a total of 13 countries have Gavi approval to introduce HPV routine programmes before the end of 2025, and 17 countries have been approved to launch MACs before the end of 2025, including those that were previously delayed from 2024 to 2025 due to supply shortfalls. If all the approved routine introductions and MACs launch on time, the programme would meet the target of 27 routine launches and 28 MAC launches in the Gavi 5.1 strategic

period. The indicator is marked as amber to reflect the risk that one or more of these launches could be delayed to 2026.

As a result of the increasing number of launches forecasted in 2025 in the v22, including a large launch in Pakistan, the forecasted VIGs and Ops expenditure in 5.1 has increased in the v22 compared to previous forecasts. Therefore, VIG and Ops disbursement as a proportion of forecasted 5.1 expenditure (now 56%) has decreased compared to the last Board report, due to the increase in denominator. This indicator is marked as amber to reflect a discrepancy against the 2024 milestone of 74%. Overall, the change represents overall an increase in 2025 launches in the HPV forecast caused by postponements from 2024 into 2025 due to the supply shortfall for 5 countries, and due to earlier forecasted launches.

Rapid adoption of the permissive, off-label single-dose schedule has continued, with 14 countries having switched from a 2-dose to a 1-dose schedule to date (4 since May 2024). In addition, 7 countries have introduced HPV vaccine on a single dose schedule, including the recent introduction in Timor-Leste. A further 25 countries, including both Gavi54 countries and MICs receiving Gavi support for their HPV programmes, have made the decision to switch or introduce with the single dose schedule in Q4 2024 or 2025. WHO analysis of the 2023 coverage data showed that countries that switched to a single dose regimen achieved an average 8% increase in HPV1 coverage. Further, modelling conducted by the Institute for Disease Modelling indicates that rapid adoption of the single-dose schedule has released enough doses to target over 24 million addition girls in Gavi-supported HPV programmes between 2023-2024, compared to a supply-constrained scenario where all countries were using two-dose schedules. Countries' rapid adoption of the single-dose schedule is enabling the achievement of the 86 million goal with available supply.

3.2 Enhanced Technical Assistance and Foundational Support

Enhanced technical assistance (TA) under the HPV revitalisation includes Targeted Country Assistance (TCA) and Foundational Support provided to WHO and UNICEF Headquarters and regional offices. To date, 33 countries either have had their TCA plans approved to access the HPV Reserve or disbursed TCA funding including from within TCA country ceilings. 26 countries were approved from the TCA HPV reserve, with a total budget of US$ 17.3 million committed. Total disbursements to date amount to US$ 7.8 million for 22 countries.

HPV TCA Reserve financial utilisation as of the second quarter is at 20% for UNICEF and 18% for WHO. Low utilisation was attributed to delayed timelines of planned MACs and introductions, due to the supply shortfall in 2024 affecting five countries. Both WHO and UNICEF indicated an expected increase in utilisation rates as implementation resumes.

To allow countries streamlined access to TA, the Secretariat conducted a Request for Proposals (RFP) process to implement comprehensive 6-year HPV TA framework agreements (2024–2030) with implementing partners. During this process, 56 partners

submitted bids to support eligible countries in a preliminary competitive phase. 19 partners were pre-selected to potentially provide technical assistance to 41 eligible countries with existing or planned HPV programs, with specific technical areas and countries delineated in the agreements, with specific activities to be specified in call off contracts. Countries can fund these TA supports through the HPV TA reserve until end of 2025 or through their TCA country ceilings. Alliance core partners retain the ability to access the HPV TCA Reserve through a dedicated contracting pathway.

Foundational Support for HPV amounts to US$ 3.6 million to WHO and an overall allocation of US$ 4.39 million to UNICEF. As of August 2024, a total of US$ 3.9 million was disbursed to both UNICEF and WHO.

UNICEF has leveraged its funds to augment its US$ 10 million HPV-Plus dedicated support to 21 countries and its mainstream programmatic support to countries for HPV vaccine programs. UNICEF is actively supporting the HPV-Plus initiative by revitalising efforts to increase vaccination uptake. It is leveraging its multisectoral programming to deliver services on nutrition, sexual and reproductive health (SRH), mental health, menstrual health and hygiene, and violence prevention. To achieve this goal, UNICEF focuses on evidence generation, cross-country learning, and nationwide scale-up planning to support the well-being of adolescent girls. UNICEF has also provided support to countries, including Angola, Ghana, Pakistan, India, Nepal, Mali, Timor-Leste, Bangladesh, and Zimbabwe to introduce HPV vaccines and implement MAC campaigns. Additionally, for H1 of 2024, UNICEF has delivered 27.98 million doses of HPV vaccine to 37 countries and territories.

Despite setbacks due to supply shortfall, Foundational Support through WHO supported HPV coverage improvement efforts. A prioritisation framework was developed for secondary targets, with support provided to several countries including Tanzania and Zimbabwe through planning and technical assistance support. Through coordination with partners like UNICEF, Gavi, and Bill & Melinda Gates Foundation, WHO disseminated the indication on one dose use for Innovax HPV2 vaccine (Cecolin) through the update and dissemination of the Considerations for HPV Vaccine Product Choice guidance. In addition, 96% of Gavi countries with HPV programmes successfully reported 2023 HPV data under the WHO and UNICEF Estimates of National Immunization Coverage (WUENIC) HPV estimates.

3.3 Health Systems Strengthening Update

Gavi's HPV revitalisation programme continues to support countries to improve routinisation and HPV vaccine uptake through Health Systems Strengthening (HSS) grants. During this reporting period, no country requested to reallocate their existing HSS grants; instead, all countries requested additional HPV funding. Gavi approved top-up requests through internal Secretariat review from The Gambia (US$ 0.4 million), Côte d'Ivoire (US$ 0.75 million), Senegal (US$ 0.5 million), and Liberia (US$ 0.65 million). A US$ 4 million top up for Nigeria was recommended for approval by the IRC as part of the Full Portfolio Planning (FPP) request. The type of activities supported varied with country context. After acquiring additional HPV

vaccines, The Gambia used HSS funding to complement The Big Catch-Up through integrated demand generation activities. In Côte d'Ivoire, HSS funds were used to complement operational costs for the delayed MAC, meet outreach costs and create demand for HPV vaccination. Nigeria will utilise HSS funds to integrate HPV vaccination into its Maternal, Newborn and Child Health week and to initiate annual school-based vaccination campaigns called "Green October". To date, US$ 11.9 million of HSS has been approved for use towards HPV revitalisation. It is important to note that funding comes from within HSS, this means no financial impact for the overall consolidated forecast.

Relying on HSS funding to cover operational costs for delivering HPV vaccines poses a risk to the programme as it dilutes the potential impact HSS funding has on health systems strengthening. Although Gavi will achieve near-term targets, countries will likely continue to face challenges in meeting operational costs with current financing structures and service delivery methods. This uncertainty will persist with funding lever consolidation and the move towards targeted and catalytic approaches in Gavi 6.0.

3.4 HPV Learning Agenda

Alliance partners have a coordinated approach to HPV learning and the Secretariat's HPV Learning Agenda is complemented by other partners' investments, including Bill & Melinda Gates Foundation, UNICEF, and Unitaid. The UNICEF HPV-Plus initiative, notably the pillar on integrated programming creates a significant learning opportunity for HPV vaccine delivery, with integration components spanning across SRH, human immunodeficiency virus (HIV), mental health, and nutrition among others. The Gavi Learning Agenda has advanced considerably since April 2024 across three learning themes: i) integrated services for adolescents; ii) strengthening HPV coverage measurement; and iii) integrating adolescent girl HPV vaccination with cervical cancer screening for adult women.

- Theme 1: Between May-July 2024, seven multi-country implementation research projects under the Strategic Focus Area (SFA) launched to test how **integrated service delivery approaches** could increase HPV coverage equitably and sustainably, as well as contribute to wider adolescent health outcomes. Implemented in 11 countries, the studies cover a diverse mix of delivery channels (i.e. school, facility, community), platforms (i.e. immunisation, human immunodeficiency virus), service integration (i.e. education, screening), designs, and country contexts (i.e. Africa, Asia). All projects have rapidly launched and are pursuing ethics approval before data collection (~Q4 2024) and service implementation begins (~Q4/Q1 2025). Projects are scheduled to be completed by December 2025. In addition, a cross-portfolio knowledge translation project was awarded to help Gavi and stakeholders learn and synthesise insights across projects, countries, and contexts.

- Theme 2: Alliance partners have collectively recognised the need to strengthen **HPV coverage measurement** for administrative data validation and to identify alternative approaches that are less time and resource intensive. Gavi and the

Bill & Melinda Gates Foundation are co-funding a project across three countries (Liberia, Senegal, Rwanda) to help define optimal survey methodology, conduct "traditional" population-based coverage surveys, and to compare the results to "innovative" coverage survey approaches. Currently under contracting with the lead bidder, the project is expected to start by the end of October 2024 with Gavi's contract ending November 2025 and Bill & Melinda Gates Foundation's contract ending September 2026.

- Theme 3: HPV vaccination is a core pillar of the cervical cancer elimination strategy, along with screening and treatment. Anticipating a small amount of uncommitted HPV learning funds, Gavi has partnered with Unitaid to strengthen understanding of the potential linkages across these pillars. Leveraging Unitaid's existing investments in cervical cancer screening and treatment programmes, Gavi will fund one Unitaid-supported partner to test how service models **that integrate delivery of HPV vaccination for girls and cervical cancer screening services for women** might increase HPV vaccination coverage, as well as contribute to women's health outcomes. The restricted RFP is in negotiation, with the project to run from November 2024-November 2025.

By end of September, 71% (US$ 11.6 million) of the US$ 16.24 million HPV learning agenda budget has been committed with US$ 530,000 disbursed as of 30 September 2024, all related to Theme 1. Upon award of the remaining two learning projects, all US$ 16.24 million HPV SFA funds are projected to be committed with near full disbursement by December 2025.

3.5 Advocacy to Accelerate HPV Introductions

In support of HPV revitalisation, advocacy activities continued at national, regional and global levels. Gavi supported the continental launch of the Organisation of African First Ladies for Development (OAFLAD) #WeAreEqual campaign in May, which focuses on the health and wellbeing of women and girls including access to the HPV vaccine. The Nigerian Chapter was hosted by the First Lady of Nigeria, Senator Oluremi Tinubu, with the participation of 10 African First Ladies. In May, Gavi partnered with the Nigerian Governor's Forum to leverage the role of State First Ladies across 21 states as champions for promoting HPV vaccine access among adolescent girls as well continued advocacy engagement and policy commitment beyond introduction. The Gavi and International Vaccine Access Center (IVAC) partnership in Nigeria facilitated advocacy and social mobilisation for civil society and youth-led organisations at national and subnational levels. 16 youth champions conducted cascade training across 16 states, resulting in the activation of 153 additional ward-level vaccine champions for community sensitisation. In Timor-Leste, social mobilisation activities in 14 municipalities involved sensitisation activities with advocacy partners.

At the regional level, Gavi and Alliance partners co-hosted a side event at the WHO AFRO Regional Committee in August 2024 to promote integration of person-centred prevention and care of cervical cancer among Member States. On the margins of 77th World Health Assembly, Gavi convened HPV Alliance advocacy leads to align on

joint advocacy activities and priority countries to sustain the acceleration of cervical cancer elimination. Furthermore, Gavi is collaborating with UNICEF to outline context-specific HPV messaging to support introductions and for continued awareness among adolescents leveraging the findings of the UNICEF U-report survey that engaged over 400,000 adolescents globally to understand awareness and behavioural trends related to HPV vaccine uptake.

3.6 Middle-Income Countries (MICs) approach

In 2024, the implementation of the MICs strategy for HPV scale up progressed by providing technical and catalytic support at the country level and leveraging the Foundational Building Blocks at the global and regional levels.

Country level technical and catalytic support: Since April 2024, in addition to the launch in Timor Leste, mentioned above, the Gavi Alliance, has continued to assist with the rollout of HPV vaccine introduction in Eswatini and Indonesia, closely monitoring the implementation of technical assistance. As of 2023, over 725,000 girls aged 9- 14 years old were fully immunised with HPV vaccine with MICs Approach support, including over 676,000 in Indonesia and over 49,000 in Eswatini. In addition, four other MICs have had their applications approved and are progressing towards vaccine introduction in the coming months.

Foundational building blocks – highlights of technical assistance implemented by partners working at regional and global level: In the Middle East and North Africa (MENA) region, significant efforts have been undertaken to support advocacy and decision-making for the introduction of the HPV vaccine, as it is yet to be introduced by most countries in the region. A key workshop was organised by the WHO Regional Office for the Eastern Mediterranean in Cairo in May 2024 to enhance the awareness and capacity of professional groups, civil society organisations (CSOs), and government officials from non-Gavi eligible MICs. The event facilitated sharing among participants from countries such as Egypt, Iran, Jordan, and Tunisia, all of which have yet to introduce HPV vaccines. Also in the region, UNICEF is supporting for advocacy and decision-making towards the introduction of HPV vaccine in Tunisia, Jordan and Egypt.

In the LAC region, UNICEF is supporting countries to design and implement behaviour insights studies to understand drivers and barriers to HPV vaccine (Bolivia, Honduras, Nicaragua), while PAHO is providing support to the development of national cervical cancer elimination plans. The East Asia and Pacific Regional Office is actively conducting analyses to understand barriers to vaccine introduction, assess financing needs, explore procurement options, and map out in-country capacities for New Vaccine Introductions (NVIs), including costing, decision-making, and implementation processes.

UNICEF HQ is working together with regional offices to support countries to use cost- effectiveness data to support HPV vaccine introduction decision-making. WHO HQ is working in partnership with regional offices to support decision-making for new

vaccine introduction, including HPV, through building the capacity of National Immunization Technical Advisory Groups (NITAGs) and other technical decision-making bodies, and strengthening access to, and use of, market intelligence to inform product choice.

Learning activities: A special HPV vaccine introduction session was held as a part of the MICs learning forum in April, which brought together government representatives from nine middle-income countries, along with partners working at the country, regional, and global levels, to share their experiences, challenges, and successes in introducing new vaccines.

Section 4: Supply Outlook

The HPV supply outlook continues to improve with recent confirmation of single-dose evidence for a third product and prequalification of a fourth HPV vaccine. However, HPV supply remains constrained to the extent that India's full communicated demand cannot be satisfied in 2025. Alliance partners continue to closely track and monitor the situation and work with countries to support and mitigate issues. 2025 HPV supply volumes should be sufficient to support all routine programmes and the launches that are currently planned for 2024 and 2025, including those previously delayed due to supply constraints and a partial quantity for India in 2025. The unexpected reduction in the 2024 HPV-4 volumes from the main manufacturer early in 2024 are expected to be covered in 2025, and overall it is expected that more supply will be available in 2025 than in any prior year, including quantities from three manufacturers. However, timing of supply is not yet fully confirmed, therefore there is a risk that the lead time for delivery and distribution of doses becoming available in Q4 2025 may delay some approved launches into 2026. All available supply is likely to be fully allocated, and countries that are now applying with a willingness to introduce in 2025 will likely have to wait until 2026. Therefore, supply allocation frameworks will continue to be utilised and overseen by the Global HPV Leadership Group until the situation of full supply is reached. To mitigate these challenges, Alliance partners are working together to accelerate the availability of supply from a third manufacturer, through an innovative market mechanism.

There have also been promising developments related to product choice. Innovax HPV-2 vaccine (Cecolin), has received WHO endorsement for single-dose use, with new data from an immuno-bridging trial indicating comparability with other HPV vaccines on a single-dose schedule, and country uptake for this vaccine has been increasing. Burundi and Tunisia have chosen to introduce using this product as an alternative to their original preference, allowing for earlier access to supply. A new HPV2 vaccine (Walrinvax) received WHO prequalification, it is recommended for two- dose schedule only and we have started the process of considering its inclusion on the Gavi menu. The Alliance is working together with external partners to disseminate awareness about HPV product choices.