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# **One dose: current guidelines, available vaccines and opportunities for MAC catchup programs with one dose**

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**CHIC SPC Symposium**

**HPV Vaccination Programs: From Pre-introduction Planning to Restoration and Sustainability**

**24 – 25 Sept 2022 – Addis Ababa, Ethiopia**

# Summary : 2017 WHO position vs SAGE 2022 recommendations

		2017 WHO position	SAGE Recommendations April 2022 <sup>1</sup>
<b>Primary target group</b>		Girls aged 9-14 years old	Girls aged 9-14 years old
<b>Vaccination Schedule</b>	9-14 years old	2-dose schedule	<b>1-dose*</b> or <b>2-dose schedule</b>
	15-20 years old	3-dose schedule	<b>1-dose*</b> or <b>2-dose schedule*</b>
	≥21 years old	3-dose schedule	<b>2-dose schedule*</b>
	Immuno-compromised	3-dose schedule (any age)	Should be prioritized and should receive at least 2 doses but ideally 3 doses, if programmatically feasible (any age)
<b>Vaccination prioritization</b>	MAC	<i>Temporarily postpone</i>	SAGE recommends countries, where feasible and affordable, <b>to prioritize catching-up missed girls through multi-age cohort (MAC) vaccination through 18 years of age</b>
	Boys	<i>Temporarily postpone</i>	Introducing the vaccination of boys and older females should be carefully managed until the global supply situation is fully unconstrained.
	Older age cohorts	<i>Temporarily postpone</i>	

<sup>1</sup> <https://www.who.int/publications/i/item/who-wer9724-261-276>

\* Off-label recommendation, girls as well as boys

**WHO position paper will be updated in December 2022 or early 2023.**



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# Trials with data on single-dose vaccination

Trial/Country	Evidence	Vaccine	Age Group	Description	Result
<b>CVT</b> Costa Rica	<u>Efficacy/</u> Immunog enicity	2vHPV	Females 18–25	<u>Post-hoc analyses</u> : participants randomized to 3 doses or control, but analyzed as 1-, 2-, 3-dose groups	<b>82.1%</b> (1 vs 0 dose) (HPV16/18) 83.8% (2 vs 0 dose) (HPV16/18) 80.2% (3 vs 0 dose) (HPV16/18)
<b>India IARC</b> India	<u>Efficacy/</u> Immunog enicity	4vHPV	Females 10–18	<u>Post-hoc analyses</u> : participants randomized to 2 or 3 doses but analyzed as 1-, 2-, 3-dose groups	<b>94.2%</b> (1 vs 0 dose) (HPV16/18) 94.5% (2 vs 0 dose) (HPV16/18) 91.2% (3 vs 0 dose) (HPV16/18)
<b>KEN SHE</b> Kenya	<u>Efficacy</u>	2vHPV 9vHPV	Females 15–20	<u>RCT</u> : 1 dose of 2vHPV, 9vHPV, vs 0 dose (MenA group)	<b>97.5%</b> (1 vs 0 dose) (HPV16/18) <b>88.9%</b> (1 vs 0 dose) (HPV16/18/31/33/45/52/58)
<b>DoRIS</b> Tanzania	Immunog enicity	2vHPV 9vHPV	Females 9–14	<u>RCT</u> : 1-, 2-, 3-dose groups <i>Bridging : Kenshe/CVT/India</i>	One, two and three doses similar (> <b>97%</b> )

Kreimer, et al. J Natl Cancer Inst 2020, Basu, et al. Lancet Oncology 2021

Barnabas, et al. April 122022, NEJM Evid 2022; 1 (5)

Watson-Jones, et al. Contemp Clin Trials. 2021 Feb;101:106266



# SAGE assessment of evidence for 1-dose

- Current evidence points to same, very high VE for 1 dose compared to 2/3
- Evidence of stable and high-quality immune response & duration of protection through at least 10/11 yr
- Sufficient strong body of evidence to make a permissive recommendation for 1 dose option

**=> Benefits for public health impact of 1-d option outweigh risks**

# *What additional evidence on 1-dose and When?*

- Impact of 1 dose in HIV+ ([n=small, HOPE, South Africa, end 2022](#))
- 1 dose Immune response through 14 & 16 years ([CVT, Costa Rica, end 2022](#))
- 1 dose VE against CIN ([INDIA - IARC, 2024](#))
- 1 vs 2 dose VE against HPV infection (non-inferiority) ([ESCUDDO 2024/2025](#))

# Products with efficacy data for 1-dose - immunobridging for new products

- “A single-dose schedule should be considered for those HPV vaccine products\* for which data on efficacy or immunobridging to vaccines with proven single-dose efficacy are available.”

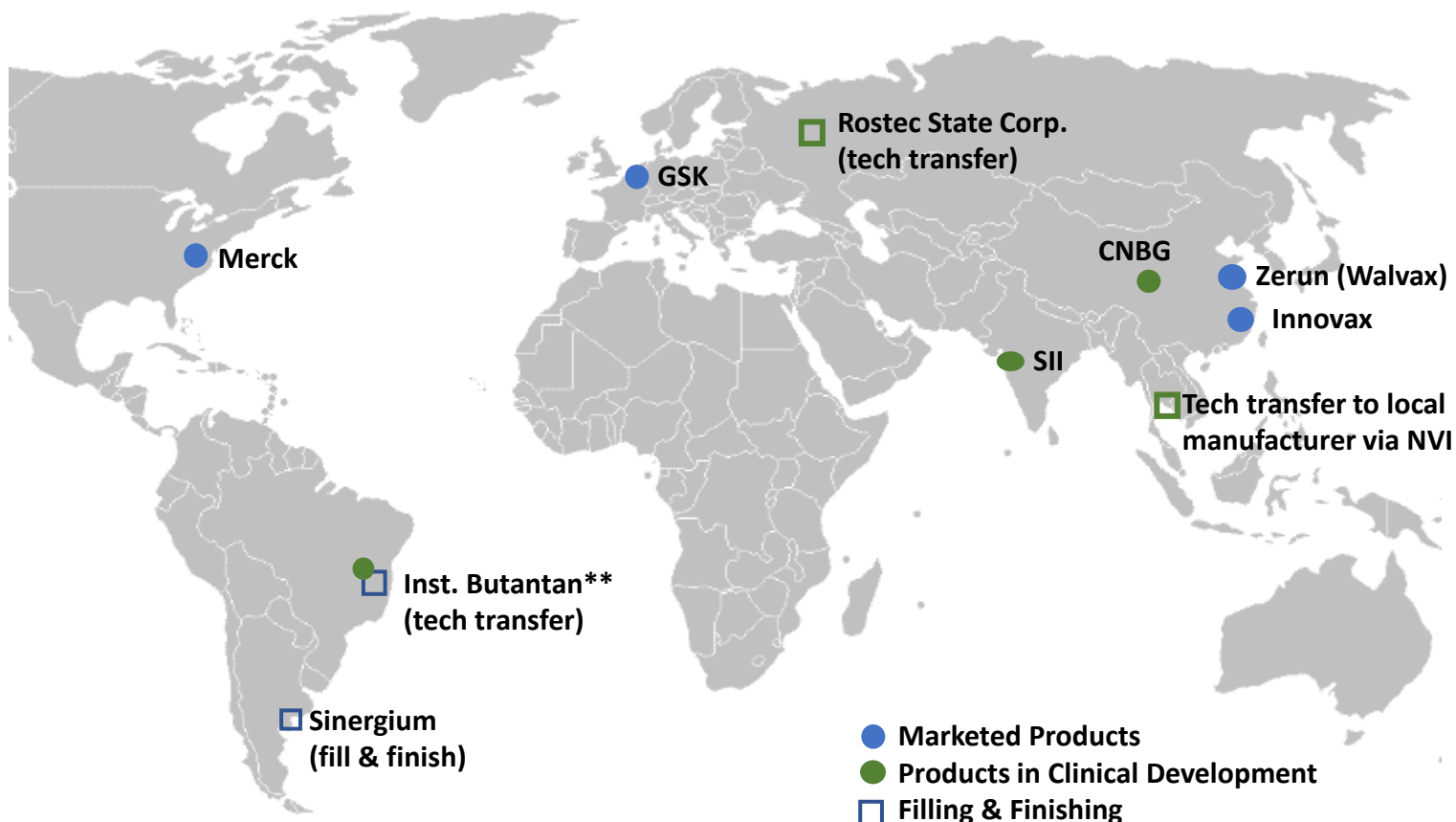
\*As per April 2022, products for which efficacy and immunogenicity data support use in a single-dose schedule include Cervarix, Gardasil and Gardasil9

- “Immunobridging refers to evidence that peak and 24-month plateau antibody levels for a vaccine are comparable to those of vaccines with proven single-dose efficacy.”

## New vaccines will require studies:

- Cecolin, Inovax - started trial with 1 dose arm comparing to Gardasil
- Wallvax, (under PQ) - no information available
- Serum Inst. ( Pre-Licensure June 2022, full licensure expected in next 6 months )-

# A supplier base in fast evolution



<b>Merck</b>	<u>Licensed globally / WHO prequalified</u> Adjuvant: Alum
Gardasil 4v & 9v	Sched.: 2 doses (9-14) or 3 doses (15+) Pres.: 1 dose vial (PQ) / PFS (non PQ)
<b>GSK</b>	<u>Licensed globally / WHO prequalified</u> Adjuvant: AS04
Cervarix 2v	Sched.: 2 doses (9-14) or 3 doses (15+) Pres.: 1,2 dose vial (PQ)/ PFS (non PQ)
<b>Innovax</b>	<u>Licensed in China / WHO prequalified (Oct 2021)</u> Adjuvant: Alum
Cecolin 2v	Schedule: 2 doses (girls 9-14) or 3 doses (women 15-45) Presentation: 1 dose vial / PFS
<b>Walvax</b>	<u>Licensed in China (March 2022)</u> Adjuvant: Alum
2v	Schedule: 2 doses (girls 9-14) or 3 doses (women 15-30) Presentation: 1 dose vial
<b>SII</b>	<u>Phase III – ongoing*</u> Adjuvant: Alum
4v	Schedule: 2 or 3 doses Presentation: 1,2,5 doses vial
<b>CNBG</b>	<u>Phase III – ongoing*</u> Adjuvant: Alum
4v	Schedule: 3 doses Presentation: 1, 3, 5 doses vial

# Despite remaining Short- term risks, global HPV supply has improved and unconstrained in the Mid & Long term

Demand Scenarios	Base Supply			Low Supply		
	Short-Term (1-3)	Mid-Term (4-6)	Long-Term (6-9)	Short-Term (1-3)	Mid-Term (4-6)	Long-Term (6-9)
2-doses (routine & MACs) <i>Base case</i>	Yellow	Green	Green	Red	Yellow	Green
2-doses (routine & MACs) & Boys	Red	Green	Green	Red	Red	Yellow
1-dose (routine & MACs)	Green	Green	Green	Light Green	Green	Green
1-dose (routine & MACs) & Boys	Yellow	Green	Green	Red	Light Green	Green



**Important assumptions of global supply/demand balance:** No mismatch between available products and country preferences

\*Single dose schedule supporting data assumed available since 2022 only for a limited number of products



# Summary of SAGE 2022 recommendations

		SAGE Recommendations April 2022 <i>WHO Position Paper (under development), expected Dec 2022</i>
Primary target group		Girls, 9-14 years old
Vaccination Schedule (F = M)	≥ 9 years old => 26/45yr	2 doses, <i>interval of at least 6m, no maximum interval*</i>
	9-20 years old	1-dose*
	Immuno-compromised & HIV+ individuals (any age)	Min 2 doses, ideally 3 doses (0, 1-2, 6m) or 6m between doses
Vaccination prioritization	MAC	Prioritize multi-age cohort (MAC) vaccination at introduction or catch-up missed girls through 18 years of age
	HIV+ & Sexually abused individuals	Prioritize vaccination of PLWHIV and children or adolescents who faced sexual abuse, including outside routine eligibility ages
	Boys	Introducing the vaccination of boys and older females should be carefully managed until the global supply situation is fully unconstrained.
	Older age cohorts	
Priority research	<ul style="list-style-type: none"> <li>Duration of protection offered by single dose in 9-14 year old girls;</li> <li>Immunogenicity and protection of reduced schedules in immunocompromised individuals</li> <li>Single dose in boys &amp; older cohorts</li> <li>Immunogenicity and protection of reduced schedules &lt;9 year old</li> </ul>	

\* Off-label recommendation



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# Countries that have announced HPV schedule optimization and adopted 1-dose

- *July 2022*
  - AFR Cap Verde (introduced in 2021):
    - Routine programme as of 9 yrs in girls 1-dose
    - Eligible group extended from 9 yr old girls to 9-14 yr old girls (catch up)
- *August 2022*
  - EUR UK (introduced in 2008) 1-dose, 9 to 25 yr girls and boys  
MSM 25+ 2 doses
  - Netherlands (from 3) -> 2 doses for 15 - 26 year in catch up
- *Aug 2022*
  - WPR Tonga (Planned introduction September 2022)
    - Introduction with 1 dose , extension of catch up ->17yr (from 14 yr earlier)
  - Solomon island (introduced in 2019)
    - Routine programme as of 9 yrs in girls 1-dose
- *NITAGs in several GAVI-eligible countries have recommended HPV application with 1-dose schedule*

# Data Sources

## HPV vaccine Dashboard (Visuals)

This dashboard provides information about the status of HPV vaccine introduction in WHO Member States. As per the Global Strategy for Cervical Cancer Elimination, each country should introduce HPV in the national immunization schedule by 2030 and meet the target of 90% of girls fully vaccinated with HPV vaccine by age 15. Detailed information on the definition and data source of each indicator can be found in the Metadata page.

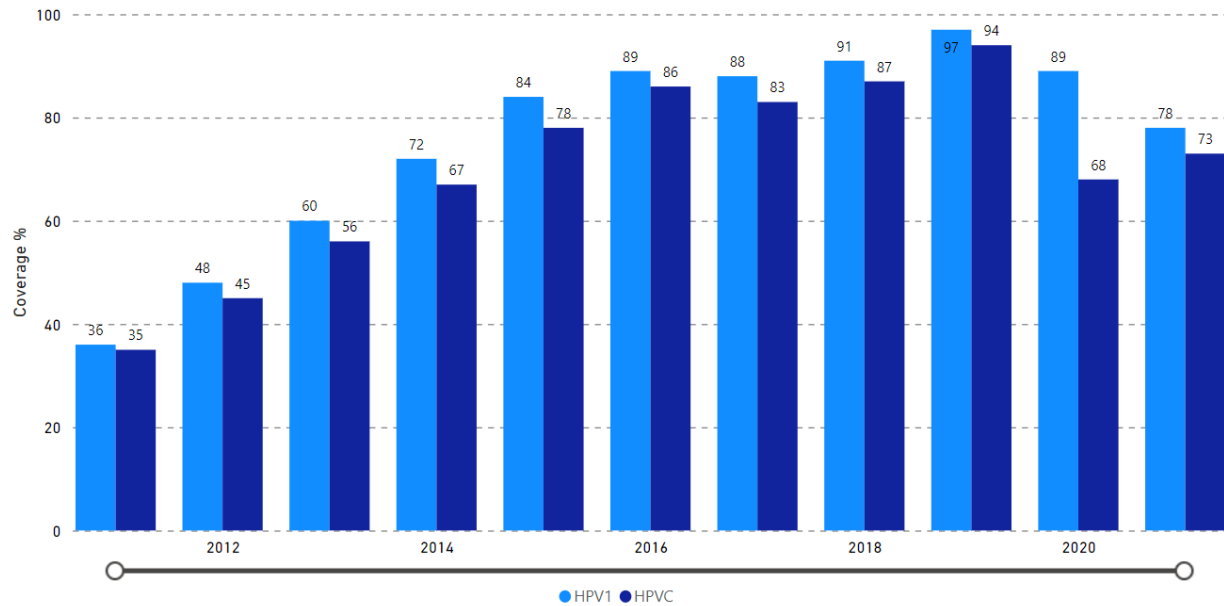


Rwanda



National schedule	Year of introduction	Delivery strategy	Targeted Age	Targeted Sex	Interval between doses
Yes	2011	School-based	12	Female	6 months

HPV vaccine, programme coverage in female



Link

<https://app.powerbi.com/view?r=eyJrIjojNDIxZTFkZGUtMDQ1Ny00MDZkLThiZDktYWFiYTdkOGU2NDcwliwidCI6ImY2MTBjMGJlLWJkMjQ0OS04MTBiLTNkYzI4MGFmYjU5MCIsmMiOjhh9>

## WHO Data Portal (Download raw data)

Country / Region	Antigen	Data source	2021	2020	2019	2018	2017	2016
Andorra	HPV Vaccination program coverage, first dose, females	HPV	83%	77%	64%	49%		
	HPV Vaccination program coverage, last dose, females	HPV	83%	77%	64%	49%		
Antigua and Barbuda	HPV Vaccination program coverage, first dose, females	HPV			10%	10%		
	HPV Vaccination program coverage, last dose, females	HPV	2%					
Argentina	HPV Vaccination program coverage, first dose, females	HPV	79%	72%	87%	88%	82%	84%
	HPV Vaccination program coverage, last dose, females	HPV	53%	46%	59%	58%	49%	56%
Armenia	HPV Vaccination program coverage, first dose, females	HPV	9%	10%	17%	6%		
	HPV Vaccination program coverage, last dose, females	HPV	0%	0%	7%	0%		

Link

[https://immunizationdata.who.int/pages/coverage/hpv.html?GROUP=Countries&ANTIGEN=PRHPV1\\_F+PRHPV2\\_C\\_F&YEAR=&CODE=](https://immunizationdata.who.int/pages/coverage/hpv.html?GROUP=Countries&ANTIGEN=PRHPV1_F+PRHPV2_C_F&YEAR=&CODE=)



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Thank you for your attention