

# Human Papillomavirus Vaccine Supply & Demand Update

**UNICEF Supply Division**

**July 2015**

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A more recent note covering Human Papillomavirus Vaccine exists. Please visit [http://www.unicef.org/supply/index\\_54214.html](http://www.unicef.org/supply/index_54214.html)

## 1. Summary

- In 2013, UNICEF began procuring Human Papillomavirus (HPV) vaccine for countries supported by Gavi, the Vaccine Alliance (Gavi) and for middle-income countries (MIC) funding their national introduction.
- Total UNICEF procurement reached 4 million doses to date (end-May 2015). This is less than originally projected, on account of delayed country introductions and the recent WHO recommendation to reduce the HPV vaccine-dosing schedule from three to two doses, decreasing projected demand by approximately one third.
- HPV vaccine supply available from suppliers through UNICEF is sufficient to meet the projected demand funded by Gavi, for the period 2015-2017, as well as projected by MICs.
- UNICEF has so far awarded quantities under long-term arrangements (LTA) and ad hoc Purchase Orders (PO) against confirmed country demand. Additional incremental awards will be made as new country demand materialises and timing for further introductions is confirmed.
- Gavi has to date approved funding for smaller-scale demonstration projects in 24 countries and nationwide introductions for three countries. UNICEF anticipates demand to increase significantly once Gavi demonstration programmes transition to nationwide introductions. Gavi anticipates ~20 countries to introduce HPV vaccine nationally with Gavi support by end-2017.<sup>1</sup>
- HPV vaccine delivery programmes across low- and middle-income countries are still in early stages of development.
- The affordability of pricing of HPV vaccines is a concern for Gavi graduating countries and MICs, including that high prices could hinder vaccine adoption.

## 2. General Brief and Background

HPV refers to a group of more than 100 highly transmissible and common viruses, primarily transmitted through sexual contact. Whereas most HPV infections are transient and benign, 13 are caused by high-risk type strains that can lead to cervical cancer in women, as well as anogenital warts and recurrent respiratory papillomatosis. Globally, cervical cancer is the second most common form of cancer in women, with an estimated 530,000 new cases a year, resulting in 266,000 deaths.<sup>2</sup> Sub-Saharan Africa, the Caribbean and Latin America account for the highest incidence rates. However, most fatalities occur in India, with approximately 123,000 new cases of cervical cancer diagnosed a year, of which more than 67,000 die from the disease.<sup>1</sup> Globally, two HPV strains (type 16 and 18) cause about 70% of all cases of invasive cervical cancer, with type 16 having the greatest potential to cause tumour development.<sup>3</sup> The HPV vaccine is the first to be developed specifically targeting the prevention of cervical cancer. However, as HPV vaccines do not prevent all forms of cervical cancer, WHO recommends ensuring cervical cancer screening.

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<sup>1</sup> Gavi, the Vaccine Alliance, *Strategic Demand Forecast Human Papillomavirus Vaccine Version 11.0*, Gavi, Geneva, May 2015, p.9.

<sup>2</sup> International Agency for Research on Cancer, *Cervical Cancer Estimated Incidence, Mortality and Prevalence Worldwide in 2012*, IARC, Lyon, December 2013.

<sup>3</sup> World Health Organization, *Human Papillomavirus Vaccines, WHO Position Paper*, WHO, Geneva, October 2014, p.488.

WHO recommends HPV immunization through the regular vaccination of girls aged 9-13 years in countries that identify cervical cancer prevention as a priority.<sup>4</sup> WHO prequalified HPV vaccine is currently available from two manufacturers, one in a bivalent form - preventing against two strains of HPV, and the other in a tetravalent form - preventing against four strains of HPV (Table 1). WHO recommends a 2-dose schedule for girls under 15 years of age with an interval of at least six months between the first and second dose. A 3<sup>rd</sup> dose is recommended if the interval between the first and second dose is less than five months or for girls above 15 years of age or girls that are immunocompromised or affected by HIV.<sup>5</sup> This recommended schedule of vaccines is the same for both products.

**Table 1 WHO Prequalified HPV Vaccines**

Manufacturer	Type	WHO PQ	Formul.	Vial	Shelf Life	VVM	Cold Chain Capacity
GlaxoSmithKline (Belgium)	Bivalent	2009	Liquid	1 ds	48 months	Type 30	57.7 cm <sup>3</sup>
		2009	Liquid	2 ds	36 months	Type 30	28.8 cm <sup>3</sup>
Merck (US)	Tetravalent	2009	Liquid	1 ds	36 months	Type 30	75.0 cm <sup>3</sup>

Source: WHO.

The US Food and Drug Administration (FDA) recently approved a 9-valent HPV vaccine manufactured by Merck.<sup>6</sup> However, the vaccine has not been prequalified by WHO. There is a requirement for all vaccines for purchase by United Nations agencies to be prequalified by WHO.

Because HPV vaccination programmes target young adolescent girls, which are a new target population for routine vaccination, delivery strategies require different approaches than most other vaccines procured through UNICEF. WHO recommends affordable, cost-effective, and sustainable approaches that are compatible with a country's delivery infrastructure and cold chain capacity, and which achieve the highest possible coverage.<sup>7</sup> Countries are still accumulating the experience and evidence from the various campaign, health facility, outreach and school-based delivery strategies. However, countries that choose to introduce HPV vaccines are encouraged to leverage the opportunity afforded by the vaccine introduction to strengthen complementary school-based health programmes, in accordance with UNICEF, WHO, the United Nations Educational, Scientific and Cultural Organization (UNESCO) and World Bank (WB) recommendations.<sup>8</sup> Schools offer a critical platform where health and education can improve and sustain child health development. School-based delivery of immunization can also complement early childhood health care, reduce school dropout rates, and diminish the likelihood of high-risk behaviour.

Gavi began providing funding support for HPV vaccines in 2013. Two introduction pathways are available to countries (Table 2). Countries with DTP3 coverage >70%, and which have demonstrated the ability to deliver HPV vaccine to adolescent girls (defined as prior experience in multi-dose vaccine delivery to at least 50% of a 9-13 year old girls target population in an average-sized district) can apply

<sup>4</sup> Ibid.

<sup>5</sup> World Health Organization, [Meeting of the Strategic Advisory Group of Experts on Immunization, April 2014 – Conclusions and Recommendations](#), WHO, Geneva, May 2014, p.230.

<sup>6</sup> US Food and Drug Administration, [FDA approves Gardasil 9 for prevention of certain cancers caused by five additional types of HPV](#), US FDA, Washington, 10 December 2014.

<sup>7</sup> WHO, [Human Papillomavirus Vaccines, WHO Position Paper](#), p.488.

<sup>8</sup> UNICEF, WHO, UNESCO, World Bank, [Focusing Resources on Effective School Health: a FRESH Start to Enhancing the Quality and Equity of Education](#), World Education Forum, Dakar, April 2000.

for national introduction support. Countries lacking such experience can apply for support to conduct smaller-scale demonstration projects to gain the experience necessary to apply for national rollout.

Table 2 HPV Vaccine Introduction Pathways<sup>9</sup>

Steps to HPV Introduction		
Step 1	Country programme eligibility must show DTP3 coverage $\geq$ 70%	
Step 2	National introduction eligibility needs to show >50% coverage of adolescent girls: based on multi-dose vaccine delivery to a target population of 9-13 year old girls in an average-sized district.	<p><b>If not possible.</b> Must demonstrate the ability to immunize a &gt;50% coverage of adolescent girls with HPV in an average-sized district over a two-year period.</p>
Step 3	National introduction	<p><b>Note:</b> Countries that choose a school-based strategy need:</p> <ul style="list-style-type: none"> <li>- 75% of the target cohort to be enrolled in school.</li> <li>- 80% of girls selected to be 9-13 years of age.</li> <li>- A vaccine strategy for girls not enrolled in school.</li> </ul>

Source: WHO.

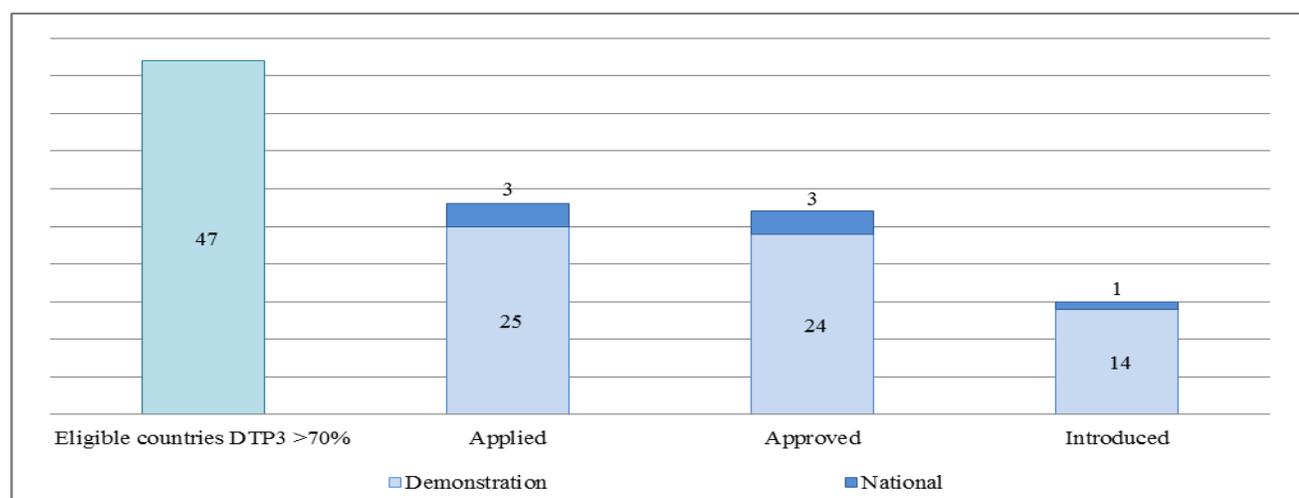
Demonstration projects will last two years, unless HPV vaccine national introduction falls in the same year as introductions for rotavirus vaccine (RV), pneumococcal conjugate vaccine (PCV) or inactivated polio vaccine (IPV), in which case demonstration projects will last 3 years. Demonstration projects expected to take place in the countries affected by the recent Ebola virus disease (EVD) outbreak, and certain large and populous countries, will also likely require 3 years.

### 3. Current Market Situation

#### 3.1. Gavi-Eligible and Graduating Country Demand

The HPV vaccine programme across Gavi countries is still in its early stage of development. Forty-seven Gavi countries are currently eligible (based on national DTP3 coverage levels) to introduce HPV vaccine with Gavi funding support. To date, 28 of these countries have applied to Gavi for HPV vaccine support. Fifteen countries have introduced HPV vaccines, of which 14 have introduced HPV vaccines into demonstration projects, and only one country, Rwanda, has introduced HPV vaccine into its national immunization programme (Figure 1).

Figure 1 Country Eligibility and Programme Status (as of December 2014)



Source: Gavi.

<sup>9</sup> Gavi, the Vaccine Alliance, [Human Papillomavirus \(HPV\) Vaccine Support](#), Gavi, Geneva, February 2014.

UNICEF has also procured HPV vaccines for three additional approved demonstration programs (Côte d'Ivoire, Liberia and Nepal), which are currently pending introduction due to programmatic delays. These three countries bring the current total demand for HPV vaccines through UNICEF to 18 Gavi-eligible countries across both demonstration projects and national introductions.

UNICEF now anticipates the total 2013-2017 country demand to reach 27.2 million doses. A revised recommended WHO HPV immunization schedule reduction from three doses to two doses, following the strategic advisory group of experts' (SAGE) conclusion of immunological evidence and advice, reduced demand.<sup>10</sup> The inherent uncertainty in country uptake and changes to national introduction timings, including large country postponements (Bangladesh, Ethiopia and Nigeria) also account for a lower demand than the 55.8 million doses initially anticipated during this period.<sup>11</sup> Figures 2 and 3 describe the changes to projected country national introduction timings from Gavi's strategic demand forecast (SDF) v.06 (2012) to SDF v.11 (2015).

**Figure 2 Anticipated National Introductions SDF v.06 (2012)**

2014	2015	2016	2017
Rwanda	Cameroon	Benin	Bangladesh
Uganda	Gambia	Burundi	CAR
	Kenya	Côte d'Ivoire	Comoros
	Lao PDR	Ethiopia	Nepal
	Malawi	Ghana	Togo
	Mauritania	Kyrgyzstan	Viet Nam
	Mozambique	Madagascar	
	Sao Tome & Principe	Nigeria	
	Solomon Islands	Papua New Guinea	
	Zambia	Senegal	
	Zimbabwe	Tanzania	
		Uzbekistan	

	Introduced
	Approved
	Not yet applied

**NB:** Figure excludes forecasted demonstration projects.

Source: Gavi SDF v.06 (2012).

**Figure 3 Anticipated National Introductions SDF v.11 (2015)**

2014	2015	2016	2017
Rwanda	Uganda	Ghana	Burkina Faso
		Kenya	Cameroon
		Lao PDR	Gambia
		Madagascar	Mozambique
		Malawi	Nepal
		Uzbekistan	Niger
			Senegal
			Sierra Leone
			Solomon Islands
			Tanzania
			Zambia
			Zimbabwe

**NB:** Figure excludes forecasted demonstration projects. National Introductions in Côte d'Ivoire and Liberia are anticipated in or after 2018

Source: Gavi SDF v.11 (2015).

### 3.2. MIC (Non-Gavi) Country Demand

Demand from self-funding countries through UNICEF has so far included the Pacific Islands, Peru, and the Philippines. UNICEF anticipates demand from these MIC countries will reach 1 million doses during 2015 and expects demand for this segment of countries to increase as additional countries consider HPV vaccine introductions.

<sup>10</sup> World Health Organization, *Human Papillomavirus Vaccines, WHO Position Paper*, WHO, Geneva, October 2014, p. 478.

<sup>11</sup> Gavi, the Vaccine Alliance, *Strategic Demand Forecast Human Papillomavirus Vaccine Version 7.0*, Gavi, Geneva, 2013.

### 3.3. Gavi-Eligible and Graduating Country Supply

UNICEF has procured 2.4 million doses for 18 Gavi-eligible countries since 2013 through to end-May 2015. The HPV vaccine quantity offered in response to a tender issued by UNICEF in 2012 is sufficient to cover the anticipated demand. UNICEF anticipates supply for Gavi-eligible countries will continue to be unconstrained through 2017.

At present, UNICEF has LTAs with both manufacturers of WHO prequalified HPV vaccine for 3.5 million doses in aggregate to cover Gavi-eligible countries' needs for the period 2013-2017 (Table 3). UNICEF has only awarded quantities to manufacturers based on confirmed demand. UNICEF made two award increments on new country demand and timing confirmation. UNICEF made one award in 2013 in favour of 10 demonstration projects and one national introduction. UNICEF made a second award in 2014 for an additional 10 demonstration projects (Table 3). UNICEF will make additional awards in 2015 and subsequent years as Gavi approves funding for new country applications to start national introductions or demonstration projects.

HPV vaccine procurement is subject up to 15-60 calendar days lead time for delivery depending on the product choice by countries, as planned and specified in UNICEF's annual forecasting exercise. Ad hoc demand materializing outside of UNICEF's annual forecasting exercise may be subject to longer lead times for delivery. Lead times for delivery are not based on country classification, but rather, based on whether HPV vaccine demand is forecasted and planned, or ad hoc and unplanned. UNICEF advises countries to forecast their requirements in advance to ensure timely delivery and to avoid any delays due to late order placements. No new prequalified vaccines are anticipated prior 2017.

Table 3 UNICEF HPV Vaccine LTA Awards for Gavi-Eligible Countries 2013-2017

Manufacturer (Country)	Initial 2013 Doses	Price per Dose	LTA Duration	Additional Awards January 2014	Total Awards
GlaxoSmithKline (Belgium)	180,800	\$4.60	5 years	+253,300	433,300
Merck (USA)	2,440,800	\$4.50	5 years	+624,480	3,065,280
<b>Total</b>	<b>2,620,800</b>			<b>877,780</b>	<b>3,498,580</b>

Source: UNICEF Supply Division.

### 3.4. MICs (Non-Gavi) Country Supply

UNICEF supplies HPV vaccine to non-Gavi countries through a MIC New Vaccine tender as well as other ad-hoc single-country tenders. To-date (June 2015) the Pacific Islands, Peru and the Philippines have been supplied at least 1.49 million doses through UNICEF. Table 4 describes UNICEF's HPV vaccine procurement on behalf of non-Gavi MICs from 2014 through 2015 to-date (June), and for country procurements over \$100,000 in value.

Table 4 UNICEF MIC (non-Gavi) HPV Vaccine Procurement 2014-YTD 2015 Over \$100,000

Vaccine	Manufacturer	Vaccine Price Range per Dose	Total Award in Doses
HPV	Merck (USA)	\$12.00-14.40	1,488,960
<b>Total</b>			<b>1,488,960</b>

Source: UNICEF Supply Division.

Unlike most Gavi-supported countries, MIC countries procuring through UNICEF self-finance the entirety of their HPV vaccine purchases. The magnitude of the price differential might serve as a barrier to vaccine adoption in some countries, or threaten the ability of some countries to maintain previously introduced HPV vaccines once they graduate from Gavi support.

MICs have self-reported to WHO's Vaccine Product, Price and Procurement project (V3P) that prices offered to countries procuring HPV vaccines directly from manufacturers range from US\$20.94 to US\$93.40.<sup>12</sup>

UNICEF is currently working with manufacturers and the countries in question to understand how it can make more transparent the prices secured for these MICs.

#### **4. Issues and Challenges**

- Changes to HPV vaccine forecast have temporarily reduced the demand on existing manufacturing capacity by a substantial volume. The change in WHO's HPV immunization schedule recommendation account for the decrease, as well as the inherent uncertainty in country uptake due to changes to national introduction timings and country postponements.
- Many delays in HPV vaccine introduction are due to country programmatic readiness and competing priorities with other new vaccine introductions.
- All countries will transition from a 3-dose to a revised 2-dose schedule in the national rollout. Close dialogue is required with countries and manufacturers to ensure an accurate programme outlook and demand forecast.
- HPV vaccine price remains a concern for countries that are considering the long-term sustainability of financing programs for both self-financing and Gavi-graduating countries.
- Higher prices and uncertain financing further creates uncertainty in demand.

#### **5. Steps Forward**

- A new tender is foreseen for Gavi demand to be issued during 2017 to cover the period beginning 2018 and beyond.
- UNICEF will continue to assess country demand and identify actions to improve forecast accuracy, in addition to dialogue with manufacturers and follow the development of new products.
- UNICEF will continue to explore ways to secure affordable prices for MIC that self-finance their HPV vaccine purchases, including single-country tenders, pooled procurement, price referencing, and negotiation with manufacturers.

For further questions or additional information, please contact:

Heather Deehan  
Chief, Vaccine Centre  
UNICEF Supply Division  
+45 45 33 58 90  
[hdeehan@unicef.org](mailto:hdeehan@unicef.org)

Philipp Kalpaxis  
Contract Specialist  
UNICEF Supply Division  
+45 45 33 57 90  
[pkalpaxis@unicef.org](mailto:pkalpaxis@unicef.org)

Aadrian Sullivan  
Information Management  
UNICEF Supply Division  
+45 45 33 57 68  
[asullivan@unicef.org](mailto:asullivan@unicef.org)

Other UNICEF information notes can be found at [http://www.unicef.org/supply/index\\_54214.html](http://www.unicef.org/supply/index_54214.html).

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<sup>12</sup> World Health Organization, *Database Reports and Analyses*, WHO, Geneva, 2015.