

# **Pentavalent vaccine (DTwP-HepB-Hib): Market & Supply Update**

**UNICEF Supply Division**

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## Pentavalent Vaccine (DTwP-HepB-Hib): Market & Supply Update May 2017

**This note provides revised information on pentavalent vaccine market demand and supply. Increased supply availability, and predictable demand through UNICEF resulted in price reductions, allowing more affordable vaccines for country programmes. Manufacturers also offered middle-income countries price parity, extending to them equivalent vaccine prices provided to countries supported by Gavi, the Vaccine Alliance.**

### 1. Summary

- UNICEF procures pentavalent vaccine for both Gavi, the Vaccine Alliance, and several countries in support of expanded programmes on immunization (EPI). Pentavalent vaccine procurement through UNICEF peaked in 2015 to reach 235 million doses for 73 eligible countries supported by Gavi, including India. In 2016, UNICEF procurement totalled 226.3 million doses.
- In 2016, twelve self-financed, non-Gavi, middle-income countries (MICs) procured 13.4 million doses, and countries having transitioned from Gavi (that no longer receive support from Gavi and fully self-finance their pentavalent) procured approximately 1.47 million doses through UNICEF.
- UNICEF anticipates total aggregate pentavalent vaccine forecast demand for 2017 through 2019 to reach 449 million doses, averaging 150 million doses a year.
- UNICEF launched a multi-phase pentavalent vaccine tender in 2016 for 2017-2019, with the outcome of halving of the vaccine weighted average price (WAP) per dose from US\$ 1.65 in 2016 to US\$ 0.84 for the tender period. The reduced pentavalent vaccine WAP will facilitate country programme sustainability, especially for countries transitioning from Gavi support, as they assume the responsibility to finance the cost of pentavalent vaccine in their immunization programmes.
- Manufacturers also extended access to reduced vaccine prices to MICs, offering these countries price parity with those receiving Gavi support.
- Concurrently, the number of World Health Organization (WHO) prequalified manufacturers increased from three in 2012 to seven. While seven manufacturers offered quantities to UNICEF, six were awarded supply, of which one is ceasing production due to the competitive situation and what in essence was a temporary 'surplus' of supply.
- Of the six companies awarded supply, five have a vaccine research and development (R&D) pipeline for poorest countries, representing a total of six products under development.
- Looking ahead, UNICEF will continue to focus on maintaining a healthy market using the healthy market framework (HMF) jointly developed by the Bill and Melinda Gates Foundation (BMGF), Gavi, and UNICEF as a guide to evaluate market health.

### 2. General Brief and Background

Pentavalent vaccine remain the cornerstone of the EPI and Gavi engagement. It provides protection against diphtheria, tetanus, pertussis, hepatitis B, and *Haemophilus Influenzae* type b (DTwP-HepB-Hib). The latter contributes to pneumonia, meningitis as well as other invasive diseases in children under five years of age.<sup>1</sup> Immunization programmes administer pentavalent vaccines in a three-dose schedule, and have replaced traditional DTP and other combinations of these vaccines (i.e. DTP-HepB) in many countries (Figure 1).

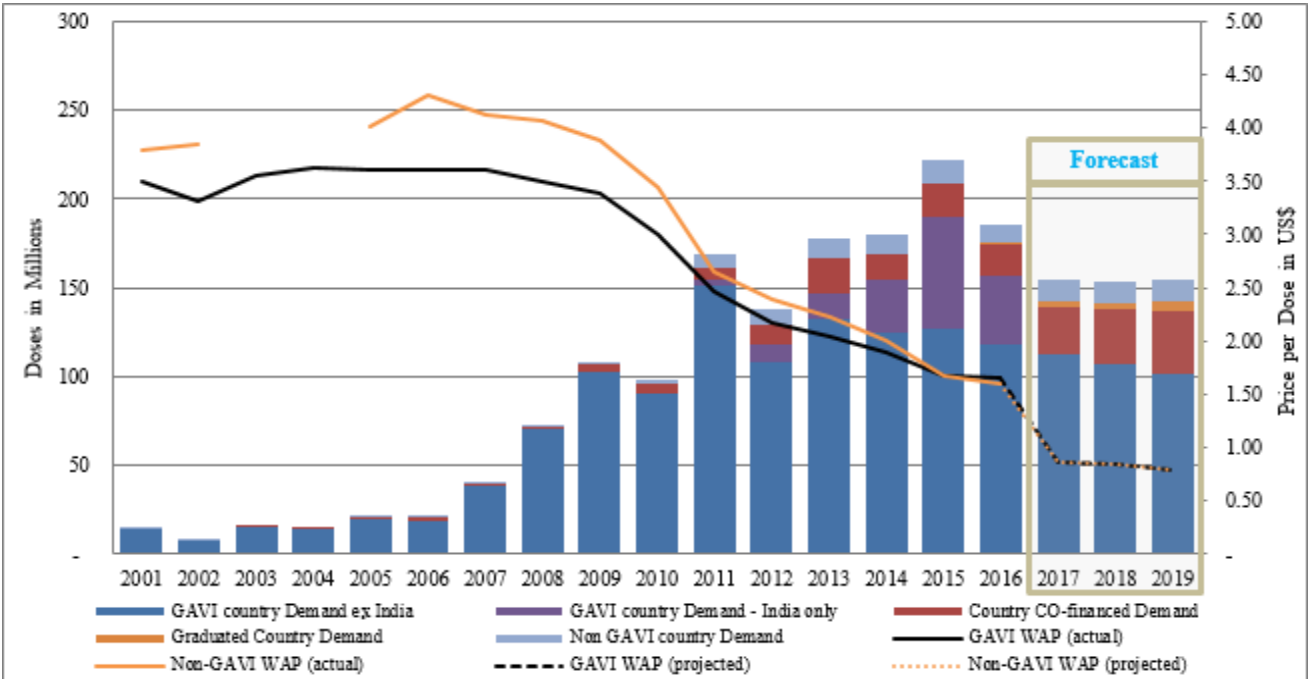
<sup>1</sup> World Health Organization, [Haemophilus influenzae type b \(Hib\)](#), WHO, Geneva, 2014.

UNICEF procures pentavalent vaccine with a whole cell pertussis component (wP), which is the vaccine used in most developing countries, consistent with the WHO’s [position paper](#) and recommendations on pertussis vaccines.<sup>2</sup> Most high-income countries use similar combination vaccines, based on an acellular pertussis (aP) component, which is currently more expensive than wP-containing vaccines and has limited global production capacity.

Since 2001, Gavi has encouraged eligible countries to immunize children against HepB and Hib by providing financial support. This fostered the introduction and expanded use of vaccines against HepB and Hib in combination with DTP through pentavalent vaccines. The support proved catalytic as it rapidly grew both the global demand for WHO prequalified pentavalent vaccine and the manufacturer supply base. Until 2006, pentavalent vaccine supply availability through UNICEF was limited, and averaged approximately 16 million doses per year. From 2007 onwards, pentavalent supply availability through UNICEF increased and the product range started to diversify (as discussed further below), and met the demand of 235 million doses in 2015 for both Gavi countries and MICs.

During the first years of Gavi’s support for pentavalent vaccines (2001-2006), only one manufacturer had a WHO prequalified vaccine. A second manufacturer with WHO prequalified vaccine entered the market in 2006, with others following thereafter. During 2010-2012, market supply was volatile, when WHO de-listed two vaccines from prequalification, and separately, three manufacturers experienced major interruptions to supply, leading to global shortages and delayed deliveries to countries.

**Figure 1 UNICEF Pentavalent Vaccine Procurement and Forecast 2001-2019**



Source: UNICEF Supply Division

At present, eight manufacturers currently have WHO prequalified pentavalent vaccines. Information and details on the different WHO prequalified vaccines can be accessed through WHO’s website [here](#).<sup>3</sup>

<sup>2</sup> World Health Organization, [Pertussis Vaccines WHO Position Paper](#), WHO, Geneva, August 2015, p. 398.

<sup>3</sup> World Health Organization, [WHO Prequalified Vaccines](#), WHO, Geneva, November 2016.

### 3. Current Market Situation

#### 3.1. Pentavalent Vaccine Supply

Not all manufacturers offer all their listed WHO prequalified vaccine presentations to UNICEF. Seven manufacturers recently offered to supply pentavalent vaccine through UNICEF, one in one-dose presentation and the remaining six in both one- and ten-dose presentations. Table 1 and 2 details some of the offered product specifications according to their presentations. UNICEF lists and ranks the manufacturers according to their cold chain volume requirements per dose, which is one of the considerations for country programmes, as existing cold chain capacity is often limited.<sup>4</sup>

**Table 1 WHO Prequalified One-Dose Pentavalent Vaccine Offers to UNICEF**

Company	Presentation	Formulation	VVM†	Shelf Life	Cold Chain
Janssen Pharmaceuticals (Belgium)	1 dose	Liquid	Type 14	36 months	10.30 cm <sup>3</sup>
Serum Institute of India (India)	1 dose	Liquid	Type 14	24 months	14.10 cm <sup>3</sup>
LG Chem (Republic of Korea)	1 dose	Liquid	Type 14	36 months	14.40 cm <sup>3</sup>
Biological E (India)	1 dose	Liquid	Type 14	30 months	14.68 cm <sup>3</sup>
Panacea Biotec (India)	1 dose	Liquid	Type 14	24 months	15.30 cm <sup>3</sup>
Shantha Biotechnics (India)	1 dose	Liquid	Type 14	24 months	16.80 cm <sup>3</sup>

Source: UNICEF Supply Division

**Note†:** Vaccine vial monitors (VVM) are heat-sensitive indicators printed on vaccine vial labels to indicate a vaccine's overexposure to heat.

**Table 2 WHO Prequalified Ten-Dose Pentavalent Vaccine Offers to UNICEF**

Company	Presentation	Formulation	VVM	Shelf Life	Cold Chain
Serum Institute of India (India)	10 dose	Liquid	Type 14	24 months	2.10 cm <sup>3</sup>
Biological E (India)	10 dose	Liquid	Type 14	30 months	2.90 cm <sup>3</sup>
LG Life Sciences (Republic of Korea)	10 dose	Liquid	Type 14	36 months	2.90 cm <sup>3</sup>
Panacea Biotec (India)	10 dose	Liquid	Type 14	24 months	3.20 cm <sup>3</sup>
Bio Farma (Indonesia)	10 dose	Liquid	Type 14	24 months	4.05 cm <sup>3</sup>
Shantha Biotechnics (India)	10 dose	Liquid	Type 14	24 months	4.40 cm <sup>3</sup>

Source: UNICEF Supply Division

Pentavalent vaccine supply availability and production capacity through 2015-2016 greatly exceeded total aggregate country demand through UNICEF. UNICEF estimates current global aggregate production capacity across all current WHO prequalified pentavalent vaccines to be 600-650 million doses a year, having increased from 400-450 million doses a year, as reported in 2015, representing an increased production capacity of 45-50%. UNICEF peak procurement reached 235 million doses in 2015, and 226.3 million doses in 2016 for 73 Gavi countries representing approximately 30-40% of the global aggregate production. Three manufacturers accounted for 85% of the supply through UNICEF of which 94% was for Gavi-supported countries (Figure 1).

#### 3.2. Gavi Demand and Forecast

From 2001 through 2006, only a lyophilized vaccine formulation was available. When WHO prequalified the first full liquid vaccine, most countries opted for that formulation. In 2010, WHO prequalified the first ten-dose vials, which became the preferred presentation by most countries. Ten-

<sup>4</sup> Vaccine cold chain volume requirements are measured on the inner carton (secondary packaging), which is used to calculate the cold chain requirements per dose in countries.

dose vials currently account for 75% of total procurement through UNICEF, and 70% of awarded quantities for 2017-2019. Country preferences trend towards a lower price and a lower effective volume per dose (Table 1-2), thereby reducing pentavalent vaccine cold chain capacity requirements and cost. Multi-dose pentavalent vaccine vials help free up space in existing country cold chain capacity, and by extension, helps to facilitate other vaccine introductions (such as PCV), avoiding the need for large capital investment to expand cold chain capacity.

UNICEF anticipates total forecast demand for one- and ten- dose pentavalent vaccine presentations to reach approximately 449 million doses during 2017-2019, representing an average of approximately 150 million doses a year (see Figure 1). The current demand forecast excludes India, as since Q2 2016 it self-procures its pentavalent vaccine requirements. This is a substantial decrease (137 million doses) compared to the volume procured over 2014-2016 totalling 587 million doses.

UNICEF recently concluded a multi-phase tender during 2016 for 2017-2019 and awarded six manufacturers 449 million doses in one- and ten-dose presentations (Table 3). Ninety percent of the forecast pentavalent vaccine demand through UNICEF is for Gavi related demand, including both the Gavi funded vaccine requirements and country co-financing obligations. UNICEF anticipates only 2% of the demand forecast will be for countries that have transitioned from Gavi support and fully self-finance their pentavalent vaccine procurement. Indications from these countries are that they will continue to channel demand through UNICEF for the time being.

**Table 3 UNICEF Pentavalent Vaccine Awards per One- and Ten-Dose Presentations 2017-2019**

	2017	2018	2019	Total Forecast
<b>1-dose</b>	48,000,000	47,000,000	45,000,000	140,000,000
<b>10-dose</b>	103,000,000	103,000,000	103,000,000	309,000,000
<b>Total</b>	<b>151,000,000</b>	<b>150,000,000</b>	<b>148,000,000</b>	<b>449,000,000</b>

Source: UNICEF Supply Division

### 3.3. Non-Gavi MIC Pentavalent Vaccine Demand

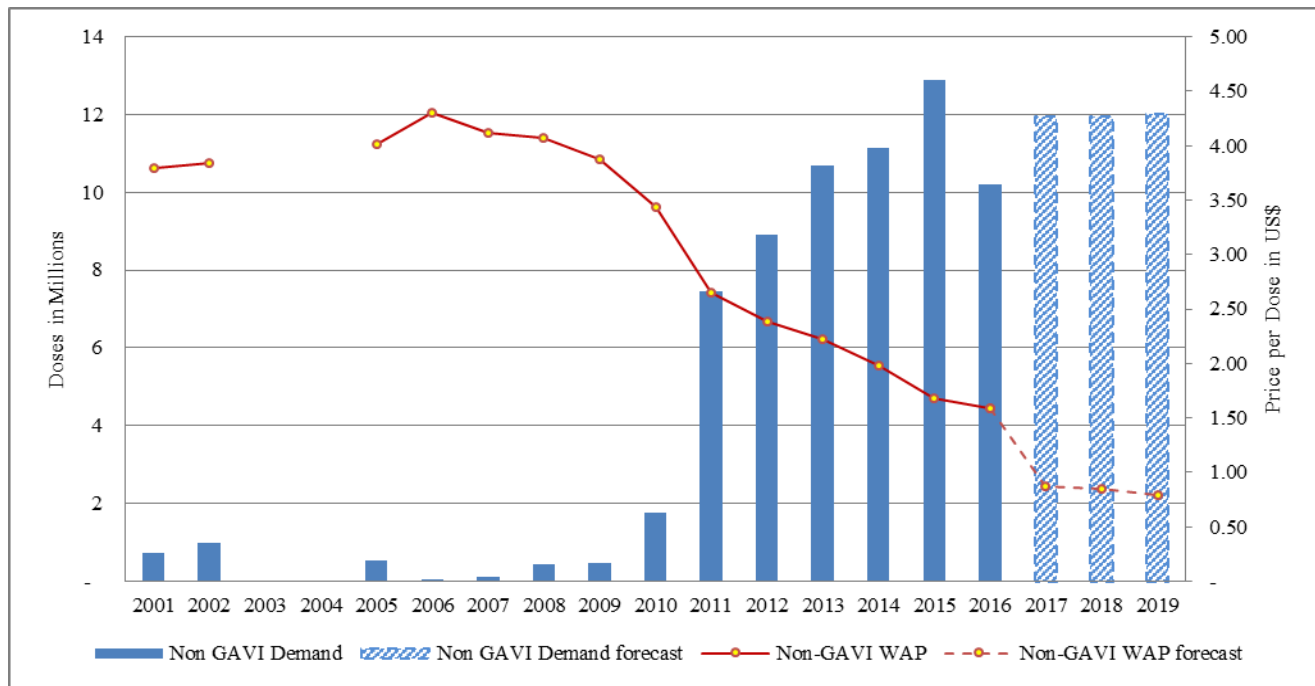
Looking beyond the Gavi-supported market segment, the demand from self-financing and MICs increased in 2010, from an average of 400,000 doses (2001-2009) to reach over 13 million doses in 2016, representing approximately 6% of total procurement through UNICEF in 2016. UNICEF anticipates the self-financing and MIC demand to reach on average 12 million doses a year over 2017-2019 (Figure 1), representing 8% of the total forecast demand (Figure 2).

The increase in total global aggregate production capacity and competition has had a positive impact on pentavalent vaccine prices for non-Gavi MICs. However, despite the aggregate forecast demand for pentavalent vaccines through UNICEF, the non-Gavi MIC demand segment remains uncertain from year to year. Most MICs tend to confirm their demand through UNICEF annually, rather than by making multi-year commitments, even though UNICEF procurement can play an important enabling role for MICs introducing these vaccines. Nevertheless, following the introduction of newer vaccines such as pentavalent vaccines, some MICs are successfully pursuing a transition phase towards self-procurement, and UNICEF anticipates the use of pentavalent vaccines by MICs to continue, even though it may not always come through UNICEF. UNICEF is working with self-procuring countries and countries transitioning from Gavi support to build capacity for strategic procurement of vaccines. This includes the Vaccine Procurement Practitioners Exchange Forum<sup>5</sup>, an annual event where

<sup>5</sup> UNICEF, [Vaccine Procurement Practitioners Exchange Forum](#), UNICEF, Copenhagen, October 2016

countries exchange their experience and best practice in vaccine procurement to ensure secure access to affordable vaccines for routine immunization programs.

**Figure 2 MIC Procurement, Forecast Demand, and WAP through UNICEF 2001-2019**



Source: UNICEF Supply Division

### 3.4. Pricing

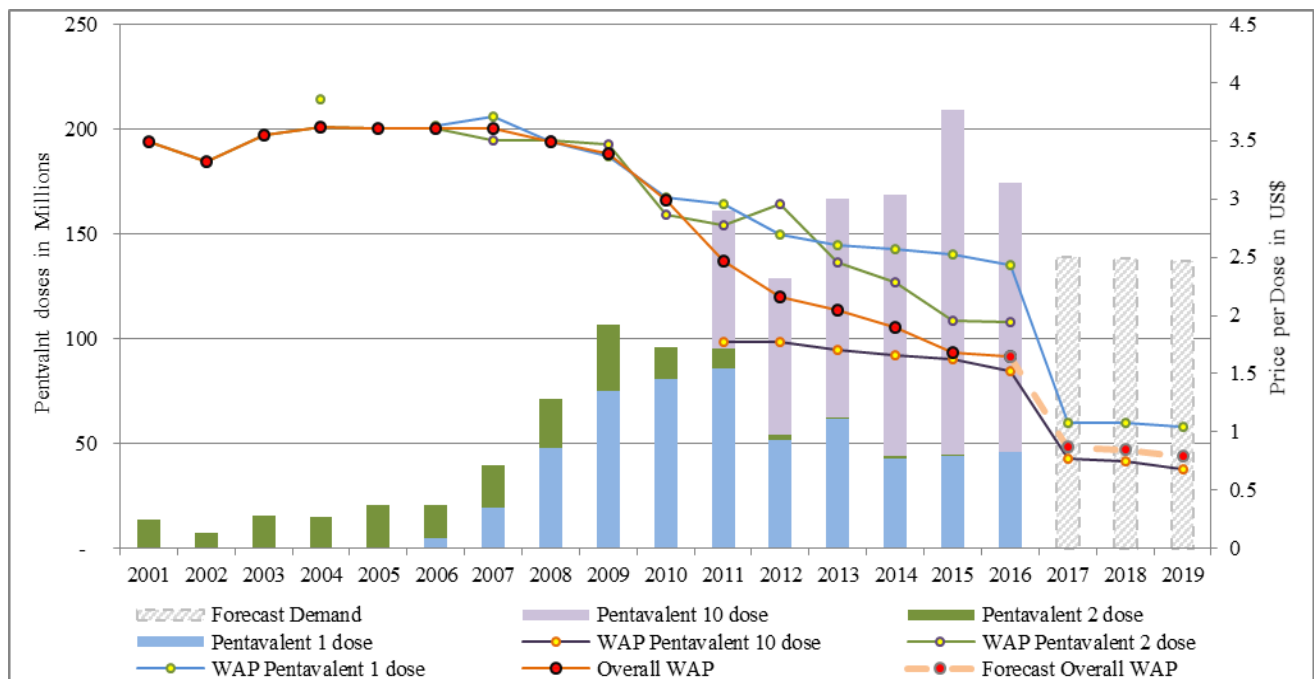
The pentavalent vaccine market’s current surplus production capacity, supply availability, and increased market competition resulted in the achievement of a number of Healthy Market Framework objectives in the current tender, notably: accommodating country presentation preferences; maintaining sufficient buffer capacity; maintaining a sufficiently diverse supply base to mitigate supplier and regulatory risks; and maintaining enough suppliers to ensure long-term competition. The tender also sought to achieve price reductions; price differential decrease between one- and ten-dose presentations; fair opportunity to access vaccine between Gavi and non-Gavi countries; and an award that represented suppliers that, as a composite, have an R&D pipeline for vaccines targeted toward the health needs of children living in the poorest countries. UNICEF launched a multi-phase pentavalent vaccine tender in 2016 for the period 2017-2019, in which a declining trend in demand through UNICEF, from a peak of 235 million doses in 2015, to an estimated 150 million doses a year during 2017-2019, was a factor (Figure 1), representing a decrease of 31%. UNICEF concluded the tender halving the pentavalent vaccine WAP per dose from US\$ 1.65 in 2016 to US\$ 0.84 for the tender period, which could result in saving donors US\$ 366 million through Gavi, and countries. UNICEF publishes vaccine prices for each manufacturer holding a long-term arrangement (LTA) with UNICEF, which can be accessed [here](#).<sup>6</sup>

Since the publication of awards and tender outcome, some manufacturers have criticized the process in terms of driving prices too low. Including those expressed by companies that may not have yet recouped investment costs incurred to establish their production lines. Price was a key factor of determining

<sup>6</sup> UNICEF, [Vaccine Price Data](#), UNICEF, Copenhagen, October 2015.

value for money procurement decisions, but as mentioned above, and as detailed below in the HMF section, price was not the only factor. Striking a balance of objectives was the basis for the awards.

Figure 3 Gavi Country Pentavalent WAP for One-, Two-, and Ten-Dose Vaccines 2004-2019



Source: UNICEF Supply Division

Figure 3 shows Gavi country pentavalent WAPs for the different vaccine presentations over 2014 through 2019. The prices published from 2001-2016 reflect those applicable to Gavi supported countries. As a result of the tender issued in 2016, manufacturers extended the same prices to all countries. The price data shows the awarded price per dose in US\$, product, manufacturer, and calendar year, based on multi-year LTAs.

#### 4. Healthy Markets Framework

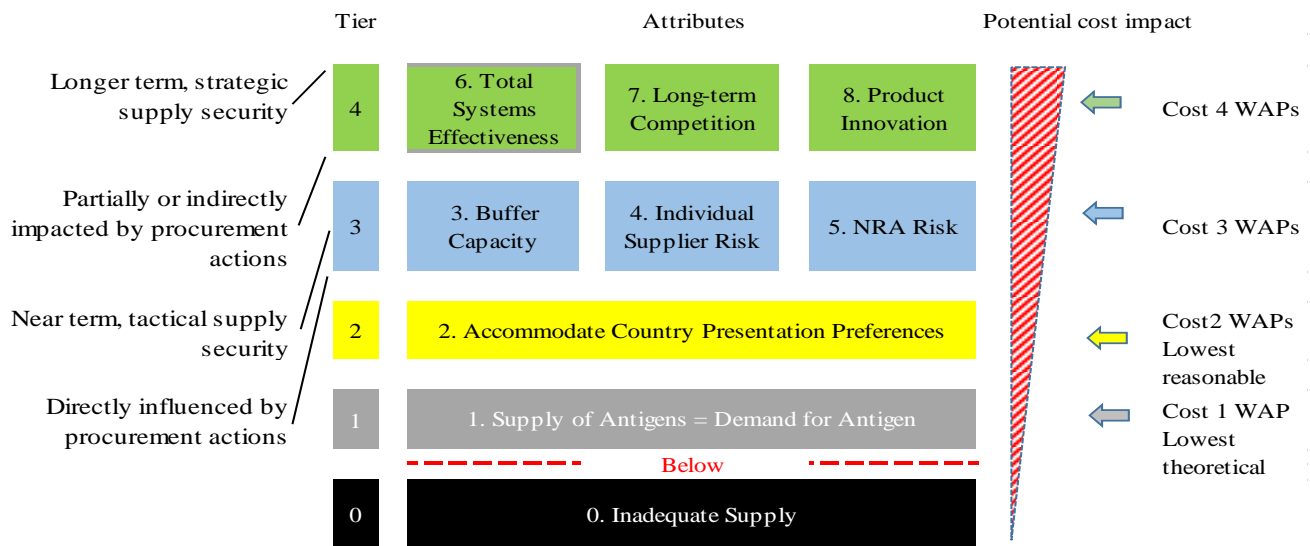
The Healthy Markets Framework (HMF)<sup>7</sup> is a tool jointly developed by BMGF, Gavi, and UNICEF to support developing country vaccine markets more effectively and consistently. The HMF describes the current state of a market and articulates an ideal future market state for vaccines and helps to ensure a common understanding of what that means for Gavi, Gavi partners, Gavi supported countries, and manufacturers, although manufacturers may have a different perspective.

Figure 4 illustrates HMF’s methodology based on the different attributes, represented by the building blocks making up the framework, the health levels (tiers 0-4), and the cost impact of attaining each level. The HMF will assist in analysing potential trade-off decisions in achieving the different elements in the market, relative to the strengths and weaknesses of the different interventions. Stakeholders can use the HMF to analyse the cost of achieving each “state”, and where possible, the longer-term costs/savings of attaining a healthy market, which will nevertheless be subject to judgement. UNICEF partners can use the HMF to establish market-shaping strategies for a particular vaccine. However, the HMF and its definition of market health focuses on market considerations for UNICEF and the

<sup>7</sup> Gavi, the Vaccine Alliance, [Vaccine Supply and Procurement Strategy 2016-2020](#), Gavi, Seattle, 2016.

countries it represents, and may not apply to other markets nor, as stated, represent the industry’s perspective of vaccine market health.

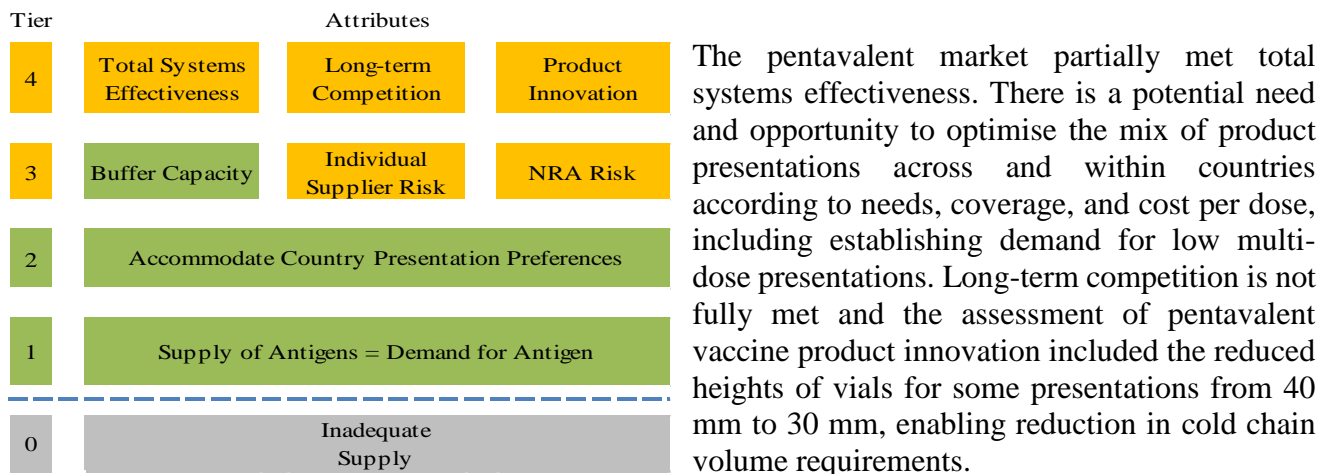
**Figure 4 Gavi, UNICEF, and BMGF’s Healthy Market Framework**



Source: UNICEF Supply Division

Figure 5 illustrates how UNICEF and partners applied the HMF to UNICEF’s pentavalent vaccine tender for 2017-2019. The analysis qualifies the pentavalent vaccine market as moderately healthy, as it adequately meets the attributes in tiers 1 and 2, as well as one of the attributes of tier 3 (buffer capacity), while it only partially meets additional attributes (in yellow).

**Figure 5 Application of the Healthy Market Framework to the Pentavalent Vaccine Market**



Source: UNICEF Supply Division

Other innovations that could contribute to improvements in immunization delivery and increased coverage have not yet materialized. Individual supplier risk (for the risk profile of individual manufacturers) is mixed. Supply concentration should remain sufficiently low, and actions taken, where necessary to maintain this level or to de-risk individual suppliers. There is a risk concerning national regulatory authorities (NRA) due to the high dependency on India’s NRA keeping its fully functional status (as per WHO classification), which will also need to be managed.



## **5. Issues and Challenges**

- The Gavi-supported pentavalent vaccine programme is maturing and demand is becoming more predictable. Until now, new country pentavalent vaccine introductions absorbed excess industry production resulting from country forecast inaccuracy, i.e. over-estimated demand forecasts from countries having already introduced the vaccine. However, Gavi-funded countries and countries that have transitioned from Gavi support, and forecasted demand through UNICEF, will require improved accuracy to avoid over-production of supply, which may in turn undermine stability in the market and affect pricing.
- A key priority for UNICEF and partners is to ensure the long-term health of pentavalent vaccine market supply. The market will continue to be dependent on multiple manufacturers.
- The Indian NRA releases over 70% of pentavalent vaccines procured through UNICEF. Therefore, the pentavalent market depends on a continued functional and effective Indian NRA to help monitor and minimise any risks to the disruption of supply.
- Despite all pentavalent vaccines currently procured through UNICEF being interchangeable, there may be programmatic challenges to switch among vial presentations. In addition, increased country-specific vaccine registration requirements can challenge product user flexibility between vaccine manufacturers to meet country programmatic demands. In order to ensure that UNICEF can meet all country requirements, UNICEF advises countries to communicate any plans to change vaccine registration requirements, or switch vaccine presentations/formulations, in a timely manner and explicitly. UNICEF advises countries to consider whether they can apply expedited registration procedures, for example relying on the WHO vaccine prequalification assessments, to ease in-country registration burdens.
- As countries transition from Gavi's pentavalent vaccine support in 2016 and onwards, and as the anticipated portion of country co-financing increases, it is important to ensure that vaccines remain affordable for countries. Maintaining fair prices will require continued competition among manufacturers, optimizing production, as well as appropriate UNICEF contracting terms.
- The demand for combination vaccines to include inactivated polio vaccine (IPV) or DTaP may materialize during the next period, particularly from MICs. UNICEF is following new IPV-containing combination vaccine innovation, and is continually trying to anticipate changes to country product preferences, while also seeking to maintain a pentavalent vaccine market with sufficient supply.

## **6. Steps Forward**

- UNICEF will continue to support manufacturers' long-term product pipeline and innovation, taking into consideration the challenges to both partners and manufacturers in projecting vaccine development timelines.
- UNICEF will continue to dialogue with industry and partners to ensure the long-term health of the pentavalent vaccine market.
- UNICEF will continue to advance and elaborate the development of the HMF in terms of qualifying and quantifying the details and defining terms and trade-offs.
- UNICEF will continue to discuss and plan with manufacturers the next tender earlier than traditionally.
- UNICEF will continue to work with countries to ensure greater accuracy in pentavalent vaccine demand forecasts based on stock levels, improved wastage rate information, and adjustments in target population and coverage assumptions.

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)

Yalda Momeni  
Contract Specialist  
UNICEF Supply Division  
+45 45 33 59 75  
[ymomeni@unicef.org](mailto:ymomeni@unicef.org)

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

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