

Yellow Fever Vaccine: Current Supply Outlook

UNICEF Supply Division

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This update provides revised information on yellow fever vaccine supply availability and increased demand. Despite slight improvements in availability and the return of two manufacturers from temporary suspension, a constrained yellow fever vaccine market will persist through 2017, exacerbated by current emergency outbreak response requirements.

1. Summary

- Yellow fever vaccine (YFV) supply through UNICEF remains constrained due to limited production capacity. Despite the return of two manufacturers from temporary suspension, the high demand currently generated from the yellow fever (YF) outbreak in Angola, in addition to potential increased outbreak response requirements in other geographic regions, outweigh supply.
- The demand in response to the current YF outbreak in Angola could negatively impact the supply availability for some routine immunization programme activities. UNICEF anticipates a constrained global production capacity to persist through 2017.
- UNICEF has long-term arrangements (LTAs) with four YFV suppliers to cover emergency stockpile, routine immunization, and preventative campaign requirements. During 2015, UNICEF increased total aggregate awards to suppliers to reach approximately 98 million doses for 2016-2017. However, whereas supply can meet emergency stockpile and routine requirements, it is insufficient to meet all preventive campaign demands, which increased the total demand through UNICEF to 109 million doses.
- The weighted average price (WAP) per dose for YFV increased 7% a year on average since 2001, from US\$ 0.39 to reach US\$ 1.04 in 2015. Given the continued supply constraints, UNICEF anticipates a YFV WAP per dose of US\$1.10 in the near-term.

2. Background

Yellow fever is an acute viral haemorrhagic disease transmitted by a mosquito vector, and causes an estimated 84-174,000 cases, and up to 60,000 deaths per year globally, of which 90% are in Africa.¹ There is no curative treatment for YF, but palliative care may address symptoms such as fever, dehydration and respiratory failure. The virus is endemic in tropical areas of Africa and Latin America, with an aggregate at-risk population of over 900 million persons, and with increasing incidence over the last two decades. While YF incidence had previously been concentrated in West Africa, it continues to spread to regions in Central and East Africa.² Eleven new countries have evidence of endemic YF, and present an elevated risk of disease outbreaks.³ Re-emergent YF is also evident in Latin America.

WHO's Strategic Advisory Group of Experts on Immunization (SAGE) recommends that countries at high-risk of YF introduce YFV into their expanded programme on immunization (EPI) as soon as

¹ World Health Organization, [Yellow Fever: Fact Sheet](#), WHO, Geneva, March 2016.

² World Health Organization, [Vaccines and Vaccination against Yellow Fever, WHO Position Paper](#), WHO, Geneva, June 2013, p. 271.

³ World Health Organization, *Meeting of the Strategic Advisory Group of Experts on Immunization, April 2013- Session 5: SAGE Working Group on Yellow Fever Vaccines*, WHO, Geneva, April 2013.

possible, and undertake preventive ‘mop-up’ campaigns, in addition to emergency outbreak response activities as needed.⁴

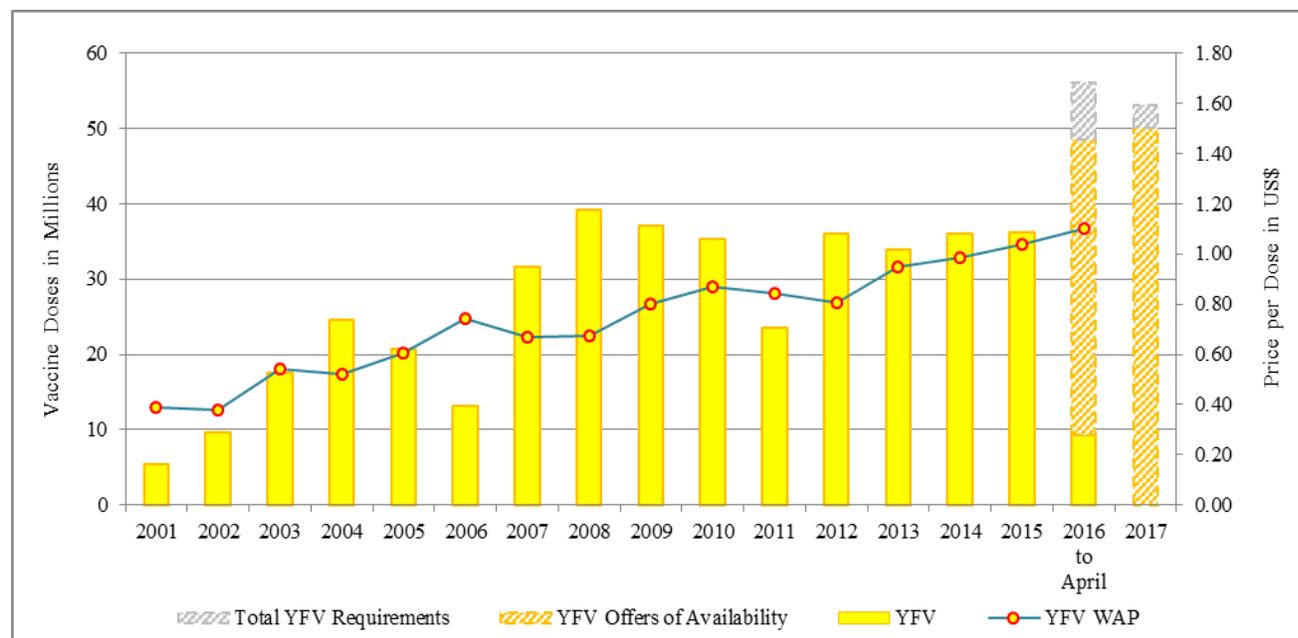
Following a global shortage of YFV in response to outbreaks in 2000, the International Coordinating Group on Vaccine Provision (ICG), set up a YFV emergency stockpile for outbreak response in 2001.⁵ The stockpile constitutes a revolving stock of six million YFV doses for outbreak response, financed by Gavi, the Vaccine Alliance (Gavi). Any unused vaccine from the emergency stockpile is used for planned preventive campaigns. The ICG, established in 1997 and made up of the International Federation of Red Cross and Red Crescent Societies (IFRC), Médecins Sans Frontières (MSF), UNICEF and WHO, coordinates and decides on the use of YFV in response to emergencies.

3. Current Market Situation

3.1 Demand

YF immunization activities are divided into three types: routine immunization, preventative campaigns and outbreak response. Over the past decade, aggregate YFV demand across all YF immunization activities increased substantially from a pre-2000 annual average of 5 million doses, to reach on average approximately 34 million doses a year since 2007. Gavi support for preventative mass vaccination campaigns, the emergency response stockpile, and introduction into a number of high-risk countries’ routine immunization programmes, has contributed to the increasing demand (Figure 1).

Figure 1 YFV Supply through UNICEF and Demand Forecast for 2016-2017



Source: UNICEF Supply Division.

Once preventive campaigns in many African high- and medium-risk endemic countries have been completed, the pressure on YFV supply should ease, such that current production capacity will be sufficient to cover the needs of routine immunization programmes and any emergency outbreak responses. By contrast, when the vaccine supply is insufficient to cover the countries’ requirements for

⁴ WHO, [Yellow Fever: Fact Sheet](#).

⁵ World Health Organization, [International Coordinating Group for Vaccine Provision, Emergency Vaccine Stockpiles](#), WHO Geneva, 2015.

all immunization activities, vaccine demand is prioritised for outbreak response followed by routine immunization programmes. Any remaining quantities are then made available to meet preventative campaign demand.

The total country demand forecast through UNICEF for all vaccination activities for 2016-2017 averages 54.5 million doses per year, and exceeds the offered availability from manufacturers by approximately 10%. The Pan American Health Organization (PAHO) forecasts requirements of approximately 15 million doses per year for the Americas,⁶ which similarly puts pressure on the balance of global supply and demand balance. The requirements for the Americas is not included in Figure 1.

Since December 2015, Angola has been facing its worst YF outbreak in three decades. Details on the outbreak and access to the latest reports issued by WHO can be found here: <http://www.afro.who.int/en/yellow-fever>. Imported cases have been reported in China, the Democratic Republic of the Congo, Kenya, and Uganda, highlighting the increased risk to other geographic regions. The emergency response requirements for the outbreak in Angola to date have reached 9.3 million doses. The spike in YFV demand has depleted the existing YFV emergency stockpile. The total requirements to control the current outbreak is not yet known, but it is expected to increase further and put more pressure on available supply.

3.2 Supply

YF vaccines are made from bulk, which depends upon sufficient specific pathogen-free (SPF) egg supply availability from which primary chick embryo cells for vaccine production are derived. Instances of limited SPF egg availability have at times curtailed vaccine production. Multiple manufacturers are currently making investments to ensure larger production capacity and supply of vaccines. Four manufacturers currently offer WHO prequalified YFV (Table 1).

Table 1 Manufacturers with WHO Prequalified YFV

Manufacturer	WHO PQ	Formul.	Presentation	Shelf life	Cold Chain Vol.	WHO PQ Status
Bio-Manguinhos (Brazil)	2001	Lyophilised	5 ds	24 months	6.31 cm ³	Active
	2007	Lyophilised	10 ds	36 months	2.96 cm ³	
	2001	Lyophilised	50 ds	24 months	0.63 cm ³	
FSUE Chumakov (Russia)	2009	Lyophilised	2 ds	24 months	7.20 cm ³	Active
	2009	Lyophilised	5 ds	24 months	6.00 cm ³	
	2009	Lyophilised	10 ds	24 months	3.60 cm ³	
Institut Pasteur de Dakar (Sénégal)	2001	Lyophilised	5 ds	36 months	2.79 cm ³	Active
	2001	Lyophilised	10 ds	36 months	1.39 cm ³	
	2001	Lyophilised	20 ds	36 months	0.69 cm ³	
Sanofi Pasteur (France)	1987	Lyophilised	10 ds	36 months	2.46 cm ³	Active

Source: WHO.

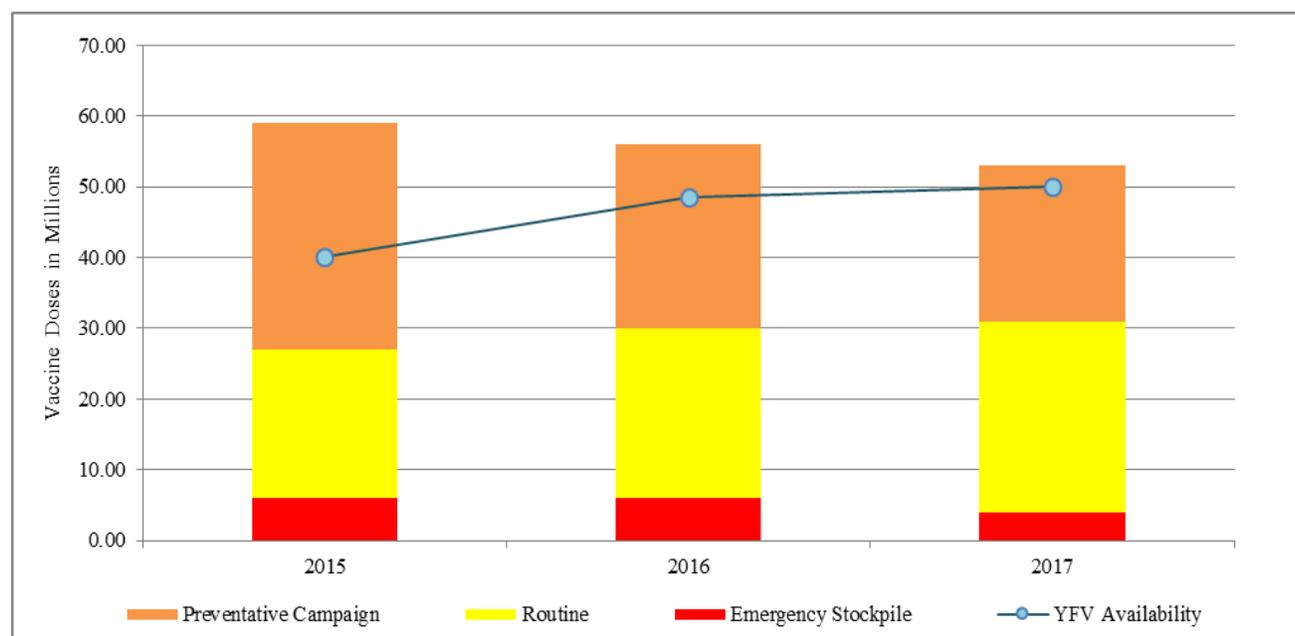
UNICEF's YFV procurement during 2015 secured 36.1 million doses for 31 countries from three manufacturers. Of these, eight million doses were for preventive campaigns in the Sudan. Supply to three of the 31 countries (DR Congo, Nigeria, and the Sudan) accounted for approximately 72% of the total volume delivered.

As of end-April 2016, UNICEF and WHO have supplied 9.3 million doses in emergency response to the YF outbreak in Angola, comprised of 6 million doses from the emergency stockpile, 2.3 million

⁶ The Pan American Health Organization, [The Pan American Health Organization \(PAHO\) Revolving Fund for Vaccine Procurement](#), PAHO, Washington, October 2015.

doses through WHO’s Revolving Fund, and a donation of one million doses from a manufacturer. UNICEF is currently securing additional doses to replenish the YFV emergency stockpile. The current priority to replenish the emergency stockpile and to ensure sufficient supply for routine immunization may reduce the quantities available for preventative campaigns. As a result, the implementation of some country preventative campaign activities may need to be postponed.

Figure 2 YFV Unconstrained Demand Forecast and Vaccine Availability for 2015-2017



Source: UNICEF Supply Division.

UNICEF increased awarded supply during 2015 by 10.6 million doses, and anticipates current offered quantities to reach 98 million over 2016-2017 (Figure 2). In 2015, the supply situation should have improved with the return of one manufacturer from temporary WHO suspension. However, the vaccine could still not be supplied to UNICEF due to lack of compliance with UNICEF requirements.

Table 2 UNICEF YFV 2015 Supply and 2016-2017 Awards

Manufacturer	2015 actual supply	2016	2017	Total
Bio-Manguinhos (Brazil)	-	8,000,000	7,500,000	15,500,000
FSUE Chumakov (Russia)	18,691,350	12,000,000	11,000,000	41,691,350
Institut Pasteur de Dakar (Sénégal)	2,058,250	7,453,880	7,603,880	17,116,010
Sanofi Pasteur (France)	19,303,100	21,000,000	24,000,000*	40,303,100
Total	40,052,700	48,453,880	50,103,880	114,610,460

Source: UNICEF Supply Division.

Note *: The supply offer from Sanofi Pasteur for 24 million doses in 2017 is subject to price negotiation.

UNICEF currently does not anticipate any new manufacturers to enter the market or seek WHO prequalification for YFV in the near future.

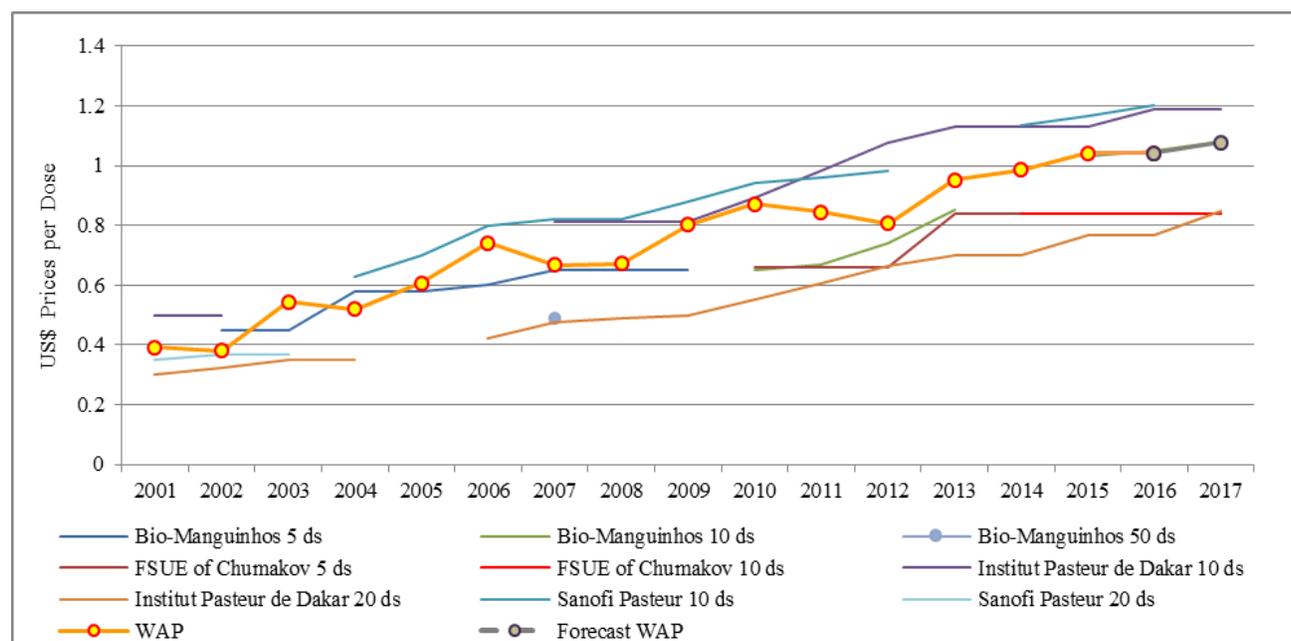
Protracted constrained availability delays important preventive campaigns, and applies additional pressure and dependency on manufacturers with limited production capacity. Close collaboration with countries and partners (UNICEF, Gavi, WHO and PAHO) is required to ensure vaccine availability for

routine immunization programmes, outbreak response, and to prioritise the allocation of limited available supply for prevention campaigns.

4. Pricing

The YFV WAP per dose increased on average by approximately 7% per year since 2001 from US\$ 0.39 to reach US\$ 1.04 in 2015 (Figure 1). Increased investment costs by suppliers to refurbish facilities and the discontinuation of 50- and 20- dose presentations have contributed to this trend. The average price of a 10-dose YFV vial increased from US\$ 0.50 in 2001 to an average price of US\$ 1.04 in 2015, representing an increase of 100% over the 14-year time period. UNICEF anticipates the WAP of YFV to reach US\$1.10 per dose over 2016-2017 given continued supply constraints and prior trends (Figure 3).

Figure 3 UNICEF YFV WAP per Dose



Source: UNICEF Supply Division.

5. Issues and Challenges

- Current YFV supply offers to UNICEF may not be sufficient to meet the necessary country requirements to implement YFV preventative campaigns. Total supply can only meet routine requirements, emergency response needs and some limited preventative campaign activities. As a result, the implementation of some planned preventative mass campaign activities may need to be delayed, spread out, or carried over to subsequent years.
- Current offers of limited supply add pressure to the management of limited supply between vaccine activities and country requirements.
- New low-risk endemic countries are expected to apply to Gavi for support to introduce YFV into their routine national immunization programmes, which could add pressure to limited supply in the short term.

6. Steps Forward

- UNICEF, together with programme partners, will continue to review YFV supply availability against demand requirements to assess and coordinate YFV allocations and prioritisation for routine, emergency response and preventative campaigns.
- UNICEF will continue to share country forecasts with manufacturers and Gavi in order to improve visibility and information on supply and demand. Countries, WHO, UNICEF and Gavi will continue to work together to conduct and finalise risk assessments to determine the need for future preventive campaigns and will plan future activities accordingly.
- UNICEF and partners will continue to explore and encourage the production of YFV through potential new manufacturers and/or support increased production capacity through all available markets.
- UNICEF awaits the outcomes of further research and normative advice on the appropriateness and feasibility of other means to manage supply constraints, such as invoking Emergency Use Assessment and Listing (EUAL) procedures, to explore unlicensed use of fractional doses and/or YFV that might be in development.⁷
- In 2017, UNICEF will issue a tender for supply during 2018 and beyond.

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Other UNICEF information notes can be found at: http://www.unicef.org/supply/index_54214.html.

⁷ Monath, Thomas. P., et al., *Yellow Fever Vaccine Supply: A Possible Solution*, The Lancet, Vol. 387 No. 10028, London, April 16, 2016, p. 1599–1600.