

Yellow Fever Vaccine: Current Outlook

UNICEF Supply Division

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Yellow Fever Vaccine (YFV) - Current Outlook

1. Key Points

- UNICEF issued its YFV 2014-2017 tender in June 2013. UNICEF had sought to maximise vaccine supply availability as well as to stabilise and reverse increases in YFV weighted average price (WAP) per dose. To date, two manufacturers have been awarded 78 million doses for 2014-2017.
- UNICEF YFV supply will not be sufficient to meet all country demand requirements for 2014-2017, and the supply remains vulnerable to persistent manufacturing difficulties. One manufacturer has recently been suspended from WHO prequalification for supply to UN agencies, including UNICEF, further reducing immediate availability.
- UNICEF's annual YFV procurement has averaged 33 million doses a year from 2007, with UNICEF procuring all WHO prequalified vaccine available to it. The original 2014-2017 requirements included in the tender averaged 62 million doses a year and exceed the offers UNICEF has received for 2014-2015 by 44%.
- YFV WAP per dose has increased by 30% a year on average since 2000, from ~\$0.20 to ~\$0.95 in 2013. The September 2013 tender awards anticipate a near-term WAP per dose of ~\$1.00.

2. Brief Background

YF is an acute viral haemorrhagic disease which causes an estimated 130,000 cases and 44,000 deaths annually in endemic African countries.¹ YF transmission is mediated by a mosquito vector, leading YF to be endemic to tropical areas in Africa and South-Central America with an aggregate at-risk population of over 900 million.² There is no curative treatment for YF, but palliative care may address some fever, dehydration and respiratory failure symptoms. WHO recommends the immunization of children through routine, preventive and reactive campaigns depending upon the risk level. Four manufacturers offer WHO prequalified YFV.

Figure 1 Manufacturers with WHO Prequalified YFV³

Manufacturer	WHO Prequal.	Presentation	Shelf Life	WHO Prequal. Status
Bio-Manguinhos (Brazil)	2001	5 ds	24 months	Suspended
	2007	10 ds	24 months	
	2001	50 ds	24 months	
Institut Pasteur de Dakar (Senegal)	2001	5 ds	36 months	Active
	2001	10 ds	36 months	
	2001	20 ds	36 months	
FSUE Chumakov (Russia)	2009	2 ds	24 months	On Temporary Hold
	2009	5 ds	24 months	
	2009	10 ds	24 months	
Sanofi Pasteur (France)	1987	10 ds	36 months	Active

Source: WHO.

¹ WHO, *Yellow Fever Burden Estimation: Summary*, WHO, Geneva, 2013, at

http://www.who.int/csr/disease/yellowfev/YellowFeverBurdenEstimation_Summary2013.pdf.

² WHO, *Yellow Fever: Fact Sheet*, WHO, Geneva, May 2013, at <http://www.who.int/mediacentre/factsheets/fs100/en/>.

³ YFV is a lyophilized, single dose schedule.

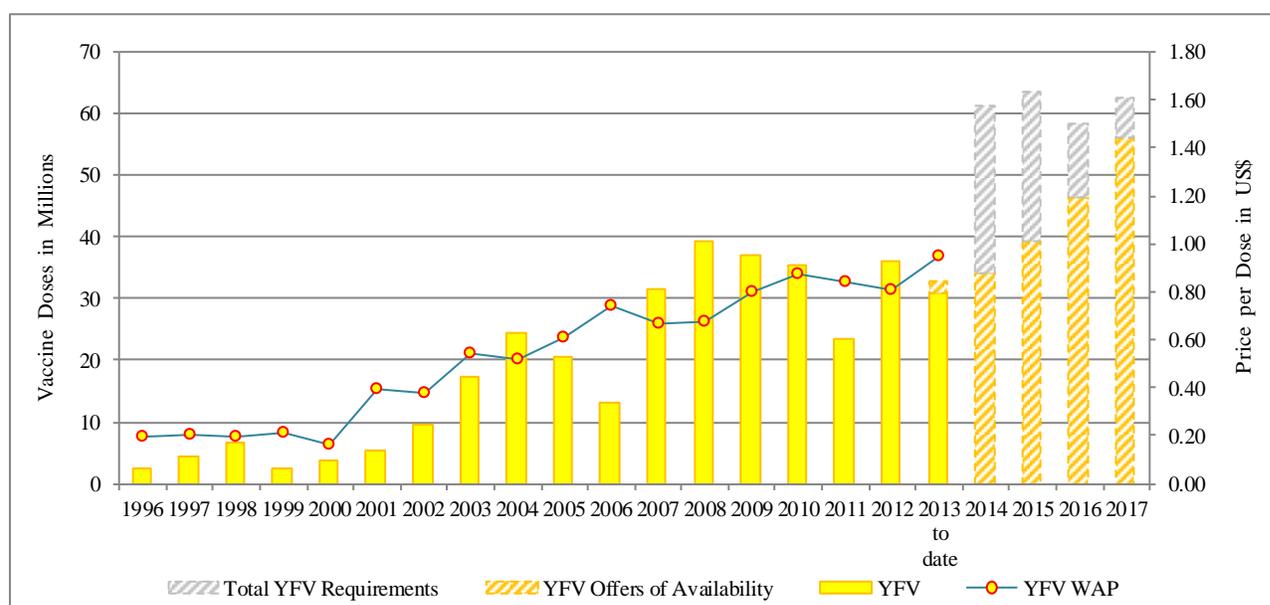
While YF incidence had previously been concentrated in West Africa, it has spread to regions in Central and East Africa.⁴ Eleven new countries have evidence of endemic YF and present an elevated risk of disease outbreaks.⁵ Re-emergent YF is also evident in Latin America. WHO's Strategic Advisory Group of Experts on Immunization (SAGE) recommends that countries with YF risk introduce YFV into their expanded programme on immunization (EPI) as soon as possible.⁶

3. Current Market Situation

3.1. Demand

Over the past decade, YFV demand has increased substantially from a pre-2002 annual average of 5 million doses. GAVI Alliance support for preventative mass vaccination campaigns, emergency response stockpiles and increased routine immunization in a number of high-risk countries since 2001 have contributed to this trend (Figure 2). Total country forecasts through UNICEF for all vaccination activities in the 2014-2017 tender averaged 62 million doses a year, which exceed current offers for 2014-15 by 44%. Increased offers made to UNICEF for 2016-17 are anticipated to reduce this gap. The Pan American Health Organization (PAHO) has also forecasted requirements of approximately 20 million doses a year, which similarly place pressure on the global supply/demand balance.

Figure 2 YFV Supply through UNICEF and Demand Forecast for 2014-2017⁷



Source: UNICEF Supply Division / GAVI SDF v.8.

⁴ WHO, *Vaccines and Vaccination Against Yellow Fever*, WHO Position Paper – June 2013, No.27, 2013, 88, WHO, Geneva, 2013, p. 271 at <http://www.who.int/wer/2013/wer8827.pdf>.

⁵ WHO, *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.

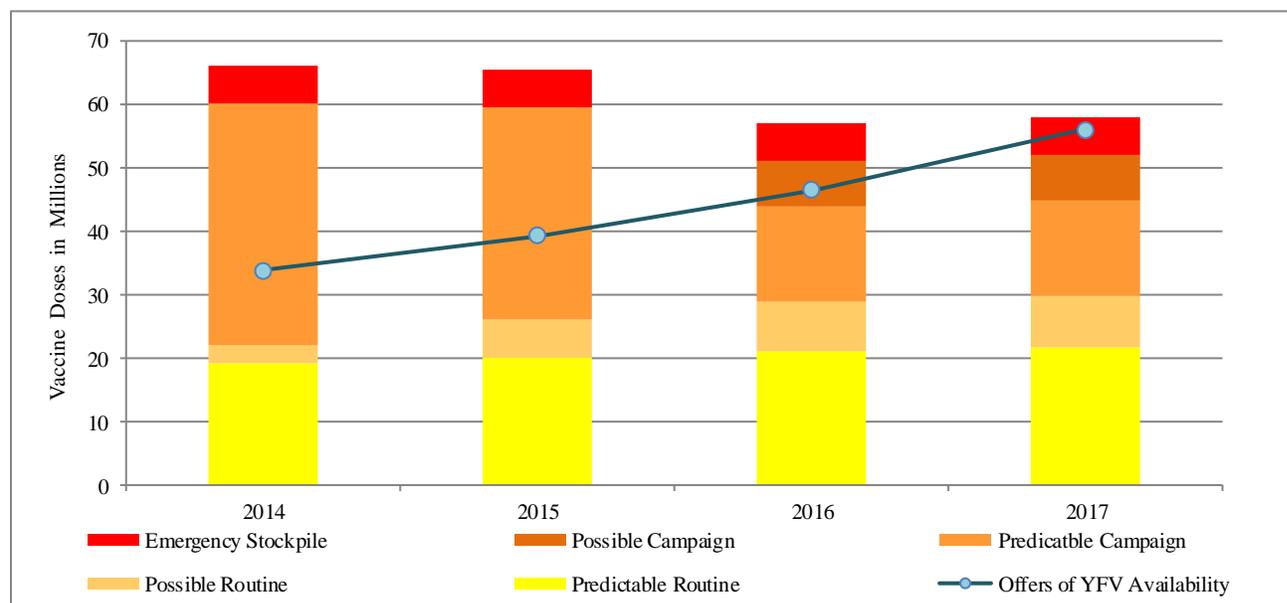
⁶ WHO, *Meeting of the Strategic Advisory Group of Experts on Immunization, April 2013- Conclusions and Recommendations*, WHO, Geneva, May 2013, Nb. 20, 2013, 88, p. 210 at <http://www.who.int/wer/2013/wer8820.pdf>.

⁷ Total YFV requirements 2014-2017 for preventative campaigns in new countries will be subject to confirmation following GAVI Board meeting decision in November 2013. UNICEF tender forecast requirements were based on GAVI SDF.v7. The chart in Figure 2 includes the most recent demand outlook provided through SDF.v8.

3.2. Supply

For 2013 year-to-date (October), UNICEF YFV procurement has totalled 31 million doses for 30 countries from the four manufacturers. Of these, 10 million doses were for preventive campaigns in Nigeria. UNICEF's current supply-constrained procurement is limited to an average of 33 million doses a year, sufficient to cover routine immunization requirements, emergency stockpiles and some limited additional campaign activities. However, offered quantities increase during subsequent years and are anticipated to approximate the originally tendered demand by 2017 (Figure 3).

Figure 3 YFV Tender Demand Forecast Requirements and Supply Offers per Activity for 2014-2017



Source: UNICEF Supply Division / GAVI SDF v.7.

That said, offered and contracted supply through UNICEF remains fragile. YFV manufacturers have experienced a number of issues affecting their ability to produce at full capacity.

- YF bulk production 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 hindered vaccine production and earlier investment necessary to guarantee increased manufacturing capacity.
- Technical difficulties have also reduced the yield of primary embryo cells from SPF egg batches which are necessary to produce adequate quantities of vaccine.
- Technical difficulties with manufacturing equipment have led to reductions in supply and the temporary suspension of WHO prequalification.
- The loss of the Good Manufacturing Practice (GMP) license by one manufacturer for one of its facilities also led to a reduction in availability and suspension of WHO prequalification.
- The increase in YFV demand from preventive mass campaigns has stretched manufacturers' capacity to supply requirements.
- The lack of clear information regarding future YFV requirements for preventive mass campaigns complicates YFV production planning which requires an 18 month lead time.

Earlier this year, although one manufacturer's WHO prequalification suspension was lifted (it had been suspended during 2012), one other manufacturer was suspended from WHO prequalification and another has been placed on temporary hold. As a result, the loss of vaccine availability could approach 13.5 million to 18.5 million doses a year (40%) in the near term. Incremental loss of availability is subject to the suspension durations, should they persist.

The reduction in vaccine availability delays important preventive campaigns and applies additional pressure and dependency on the remaining manufacturers. Close collaboration with countries and partners (UNICEF, GAVI, WHO and PAHO) is required to ensure vaccine availability for routine immunization programmes and outbreak response. As a result of global supply constraints, UNICEF, WHO and PAHO have agreed to collaborate closely together to prioritise the allocation of available supply.

Consequently, UNICEF's 2014-2017 tender exercise in July 2013 concluded with awards for the supply of 78 million doses through two manufacturers (Figure 4). The previously mentioned suspension of one manufacturer and the placement of another on temporary hold prevent UNICEF from awarding additional supply for the time being.

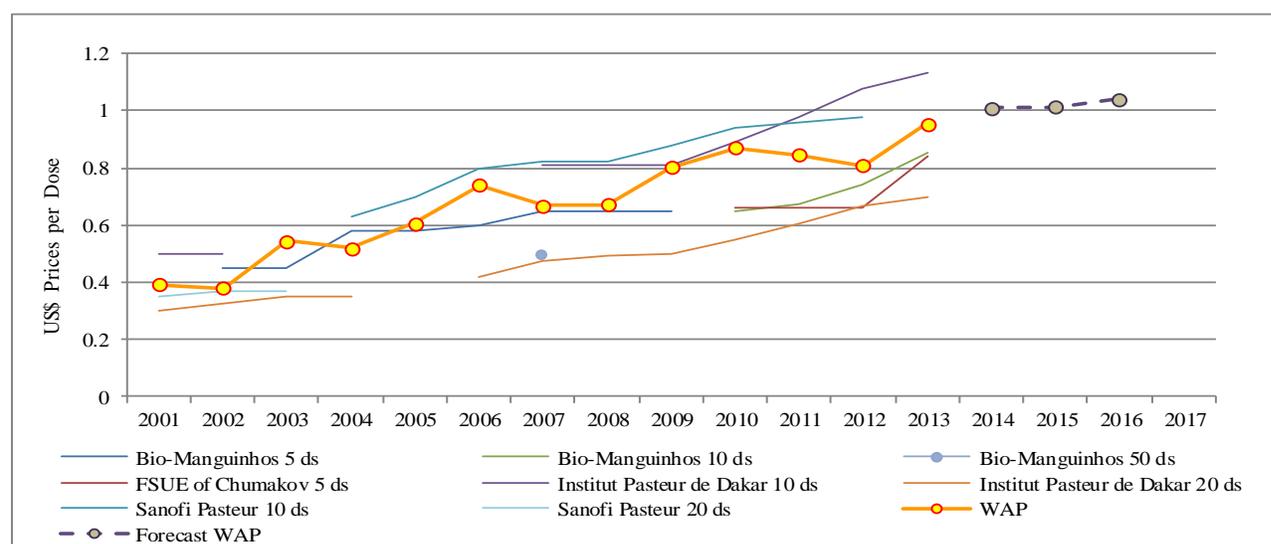
Figure 4 UNICEF YFV Quantities Awarded for 2014-2017

Company	Value	Duration	Present.	Doses	Courses
Institut Pasteur de Dakar (Senegal)	\$22,178,416	LTA – 4 years	10, 20 ds	24,340,427	24,340,427
Sanofi Pasteur (France)	\$62,985,500	LTA – 3 years	10 ds	53,500,000	53,500,000
	\$85,163,916			77,840,427	77,840,427

Source: UNICEF Supply Division.

YFV WAP per dose has increased incrementally by 30% on average a year since 2000 (Figure 1). Increased investment costs and the discontinuation of a 50 dose presentation have contributed to this trend. The recent tender awards concluded in September 2013 with a WAP per dose in the near term at ~\$1.00 for 2014-2016 (Figure 5).

Figure 5 UNICEF YFV WAP per Dose



Source: UNICEF Supply Division.

At present, UNICEF is not aware of any new manufacturers looking to enter the market and / or seeking WHO prequalification for YFV.

4. Issues and Challenges

- Current YFV supply offers through UNICEF are not sufficient to meet the total country requirements necessary to implement YFV preventative campaigns, increased routine requirements and emergency response stockpiles. As a result, the implementation of some preventative mass campaign activities will need to be delayed, spread out, or carried over to subsequent years.
- Current offers of limited supply availability add pressure on the management of limited supply between vaccine activities and country requirements.
- Over the past couple of years, country demand has been concentrated at the beginning of the year, whereas supply is limited and more readily available during the second half of the year, which has reduced programme planning effectiveness and campaign implementation.
- Once preventive campaigns in African high- and medium-risk YF endemic countries have been completed, routine EPI is expected to improve in order to maintain stable vaccination coverage rates. New low-risk endemic countries are expected to apply to introduce YFV into their routine EPI.
- The GAVI Vaccine Investment Strategy for YF (2015-2021) proposes risk assessments and preventive mass campaign vaccination to cover medium-risk endemic countries (Angola, Chad, DRC, Ethiopia, Guinea Bissau, Kenya, Mauritania, Niger, Uganda, South Sudan and the Sudan).

5. Steps Forward

- Together with partners (GAVI, WHO and PAHO), UNICEF will continue to review YFV offers and supply availability against demand requirements to assess YFV allocation and prioritisation for preventative campaigns and routine immunization.
- UNICEF, GAVI and WHO will discuss and clarify emergency stockpile arrangements and sources of funding. A WHO revolving fund has been created in order to support YF outbreak response and YFV supply.
- UNICEF and partners will continue to explore and encourage the production of YFV through potential new manufacturers through all available markets.

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Information notes can be found: http://www.unicef.org/supply/index_54214.html.