Rotavirus Vaccine: Current Supply & Demand Outlook

UNICEF Supply Division

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Rotavirus Vaccine
Supply & Demand Update – August 2013

1. Summary

- UNICEF and the GAVI Alliance have supported 9 countries to introduce Rotavirus Vaccines (RV) into their national immunisation programmes.
- GAVI has approved 20 additional countries for vaccine introduction, with procurement through UNICEF, with a combined surviving infant population of 9 million children.
- Only two manufacturers have WHO pre-qualified RV. However, one supplier has provided 90% of the supply to date (RV1), driven by country product preferences.
- Demand for RV1, a vaccine administered in a two-dose schedule, continues to exceed the manufacturer's capacity to supply. It is resulting in shortages that are likely to persist over the next 3 years, as well as delays in a number of country introductions. RV5, a vaccine administered in a three-dose schedule, retains supply availability.
- As there are no additional manufacturers expected to have vaccines prequalified by WHO in the near term, vaccine security will remain fragile.
- The 2011 tender process for 2012 to 2016 concluded with two Long Term Arrangements (LTAs) awarded for the procurement of 68 million courses (139 million doses). An additional 3 million courses were awarded in 2013 to accommodate additional demand for RV5.

2. Background & Procurement History

An estimated 1.8 million children under-five years of age die annually from diarrhoeal diseases, which is one of the leading causes of child mortality.[1] Rotaviruses are responsible for 25%-50% of severe diarrhoeal cases globally,[2] of which 90% occur in Africa and Asia.[3] More than 450,000 children under-five years of age die annually from rotavirus infections,[4] which infects nearly every child at least once before the age of five. Children aged six months to two years are the most vulnerable to infection.

WHO recommends that RV be included in national childhood immunisation programmes, particularly in countries with high child mortality from diarrhoeal disease. WHO also recommends vaccination efforts against Rotavirus complement a prevention and treatment strategy incorporating low-osmolarity oral rehydration salts (ORS), zinc supplementation and improved water, sanitation and hygiene.

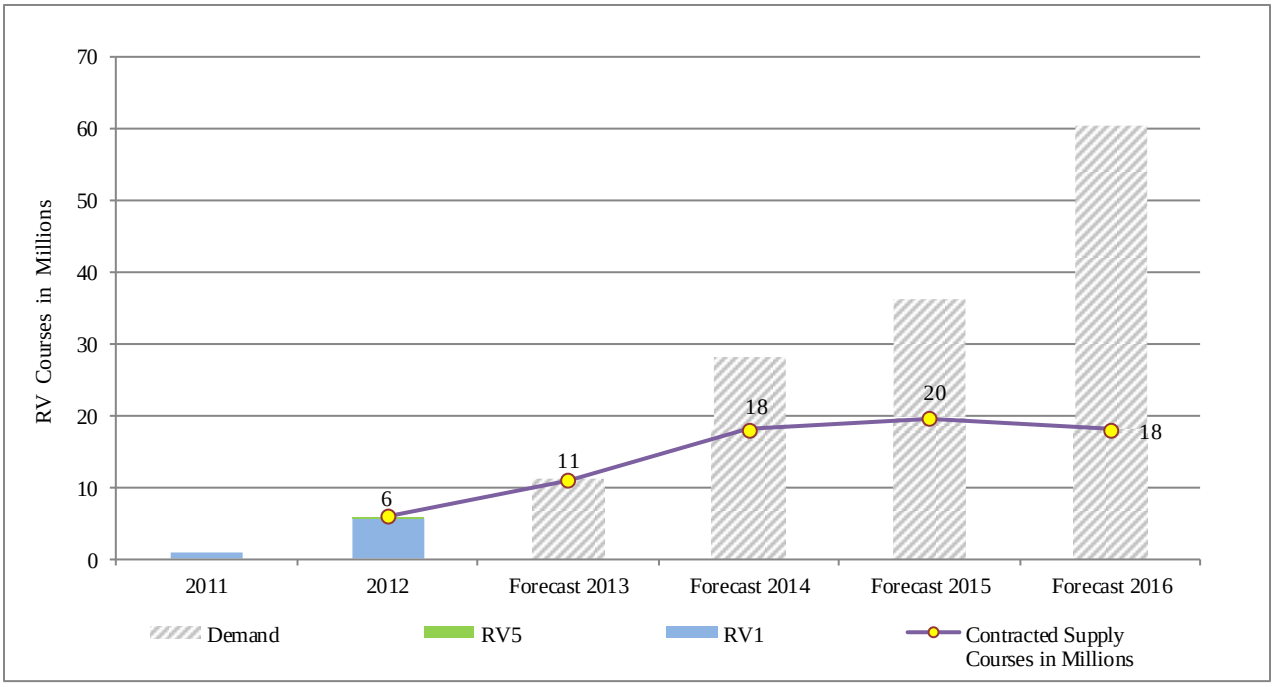
[1] WHO, *Introduction of Rotavirus Vaccines into National Immunization Programmes*, WHO, Geneva, Dec 2009, p.1 at http://whqlibdoc.who.int/hq/2009/WHO_IVB_09.09_eng.pdf.
[2] Op. cit.
[3] WHO, *Detailed Review Paper on Rotavirus Vaccines*, WHO SAGE, March 2009, p. 4 at http://www.who.int/nuvi/rotavirus/3_Detailed_Review_Paper_RotavirusVaccines_18_March_2009.pdf.
[4] WHO, *Rotavirus Vaccines: WHO Position Paper, January 2013*, Weekly Epidemiological Record, No. 5 2013 88, Geneva, February 2013, p.50 at http://www.who.int/wer/2013/wer8805.pdf.

RVs are currently available in two formulations and different presentations:

- RV1, manufactured by GlaxoSmithKline (GSK) and prequalified by WHO in 2009. A live attenuated liquid or lyophilised monovalent vaccine to be administered orally in a 2-dose schedule. It is available in a 1-dose applicator, 1-dose plastic tube and 1-dose vial presentation.
- RV5, manufactured by Merck, Sharp & Dohme Corp. and prequalified by WHO in 2008. A live attenuated liquid pentavalent bovine-human reassortant vaccine to be administered orally in a 3-dose schedule. It is available in a 1-dose tube presentation.

UNICEF procured the first doses of RV in 2011 for Sudan, the first country approved by GAVI outside of Latin America and the Caribbean. In 2012, UNICEF entered into supply arrangements with both manufacturers and expects to procure a minimum of 71 million courses, which are the current quantities under contract for 2012-2016. Incremental awards are expected as additional demand is solidified and supply is available.

Figure 1 RV Supply through UNICEF and Demand Forecast through to 2016



Source: UNICEF Supply Division.

The August 2013 demand projection in Figure 1 reflects a considerable increase in demand for 2014-2016 compared to the original February 2011 projections for country introduction which informed UNICEF's April 2011 tender for 2012-2016. In May 2011, after a one-year pause of accepting new applications due to financial constraints, GAVI received 25 country applications for financial support to introduce Rotavirus Vaccine, including five countries which were provided one last opportunity to apply before losing eligibility for financial support due to updated GNI thresholds. Compared to previous estimates, the current demand projections have increased by approximately 10 million courses for 2014 and 2015, whereas the 2016 projection has doubled. The revised 2016 demand is based upon partners' assumptions that large countries such as India, Indonesia and Nigeria will be introducing then.

3. Current Market Situation

3.1. Demand

56 countries are currently eligible for support from GAVI[5] with a combined surviving infant population of 68 million children. GAVI has approved funding support for RV introduction into the national immunisation programmes of 29 countries[6] procuring through UNICEF, with a combined surviving infant population of 17 million children, including five countries that are will graduate from GAVI support from 2016. To date, 9 countries have introduced RV, 8 additional countries anticipate introducing RV through UNICEF during 2013 and an additional 12 countries are planning RV introduction during 2014. Figure 2 presents an overview of approved and applicant countries at different stages of introduction.

Figure 2 Rotavirus Vaccine Introduction Status for Countries Procuring through UNICEF

2011	2012	2013	2014 - onwards		Countries not yet apply	
Sudan	Armenia	Burkina Faso	Angola	Lesotho	Afghanistan	Mauritania
	Ghana	Burundi	Cameroon	Uganda	Bangladesh	Mozambique
	Malawi	Djibouti	CAR		Benin	Myanmar
	Moldova	Ethiopia	Congo Rep.		Cambodia	Nepal
	Rwanda	Gambia	Eritrea		Chad	Nigeria
	Tanzania	Georgia	Guinea-Bissau		Comoros	Pakistan
	Yemen	Mali	Kenya		Congo, DR	Papua New Guinea
		Zambia	Madagascar		Cote d'Ivoire	Sao Tome e Principe
		Zimbabwe	Niger		Guinea	Senegal
			Sierra Leone		India	Solomon Islands
			Togo		Korea, DPR	Somalia
			Uzbekistan		Kyrgyzstan	South Sudan
					Lao, PDR	Tajikistan
					Liberia	Vietnam

Introduced
Approved pending introduction
Conditional approval
Countries yet to apply

The current limited availability of RV1 and the status of a country's readiness determine the timing of RV introduction. WHO, GAVI and UNICEF jointly developed a prioritisation mechanism to

[5] GAVI Alliance, *Countries Eligible for Support*, GAVI Alliance, Geneva, 2013 at http://www.gavialliance.org/support/apply/countries-eligible-for-support/.

[6] An additional four Latin American countries (Bolivia, Honduras, Guyana and Nicaragua) have introduced RV into their national immunisation programmes, and Haiti is expected to introduce in late 2013. Procurement for these countries is done through the Pan American Health Organisation (PAHO) Revolving Fund.

allocate available supply to approved countries in situations where supply is insufficient to meet the demand. The prioritisation mechanism takes into consideration factors such as disease burden and country vaccine coverage (DTP3). The anticipated readiness of countries forms the basis of planned supply. Any delay in introduction may free up doses for other countries, and therefore, this is being closely monitored. The next opportunity for countries to submit an application to GAVI for financial support is by closing date of the September 15, 2013.

So far, 25 of the 29 approved countries procuring through UNICEF have chosen to introduce RV1, mainly based on programmatic considerations. However, as a result of RV1 overall supply constraints and monthly distribution of supply plans throughout 2013, first delivery of RV1 will only be available to 13 approved countries during Q3/Q4 2013. Some are planning to introduce the vaccine in 2013, whereas others will only introduce in Q1 2014.

Figure 3 Approved Countries and Respective Vaccine Introduction Plans for 2013 and 2014[7]

2013				2014			
Q3		Q4		Q1		Q2	
RV1							
Djibouti	24,000	Burundi	255,000	Angola	715,000		
Zambia	354,000	Ethiopia	2,437,000	Cameroon	646,000		
		Zimbabwe	354,000	CAR	139,000		
				Congo, Rep	133,000		
				Madagascar	701,000		
				Niger	687,000		
				Togo	180,000		
				Sierra Leone	202,000		
Total birth cohort (surviving)	**378,000**	**Total birth cohort (surviving)**	**3,046,000**	**Total birth cohort (surviving)**	**3,403,000**	**Total birth cohort (surviving)**	**-**
RV5							
Gambia	61,000	Burkina Faso	660,000				
		Mali	645,000				
Total birth cohort (surviving)	**61,000**	**Total birth cohort (surviving)**	**1,305,000**	**Total birth cohort (surviving)**	**-**	**Total birth cohort (surviving)**	**-**

Four additional countries have been approved to receive financial support to introduce RV, three of which were approved by GAVI in February 2013. However, supply is currently not expected to be available for allocation to these countries in the near term. Regular updates are provided to these countries to ensure that planned introduction activities take into account the likely timing of supply availability.

[7] The countries listed have a collective annual birth cohort of more than 8 million children. Country introduction timing can be subjected to change. Any changes will be communicated in subsequent notes.

For those countries that have yet to apply for GAVI funding, should they request RV1, supply will only be available for national roll-out by 2015 or 2016 at the earliest. For countries requesting RV5, supply is currently available to accommodate new demand.

3.2. Supplier Base

UNICEF is procuring vaccines from the two manufacturers that have WHO pre-qualified vaccines.

- GSK has supplied RV1 through UNICEF since 2011. The vaccine is administered in a 2-dose schedule and has an approved shelf life of 36 months. It requires 34 cm³ per course of cold chain capacity and is delivered with a Vaccine Vial Monitor (VVM).[8]
- Merck has supplied RV5 through UNICEF since 2012. The vaccine is administered in a 3-dose schedule and is approved with a shelf life of 24 months. The vaccine requires a cold chain capacity of 138 cm³ per course and there is no VVM technology validated for use with this vaccine. Current available VVMs do not match the stability profile of the vaccine components. However, Merck is working with WHO to identify and assess the feasibility of a suitable temperature monitoring device for their product.[9]

Figure 4 UNICEF Awards for the 2012-2016 Tender

Vac.	Company	Value	Duration	Present.	Doses	Price/Ds	Courses
RV1	GlaxoSmithKline	€248,160,000	LTA – 5 years	1ds	132,000,000	€1.88	66,000,000
RV5	Merck	$57,162,350	LTA – 5 years	1ds	16,332,100	$5-3.50	5,444,033

Source: UNICEF Supply Division.

There are several other manufacturers developing RV in different formulations and presentations with timing for WHO-prequalification expected from 2016 at the earliest.

4. Issues / Challenges

- From 2011 to 2012, the overall supply of RV covered the needs of 8 countries procuring through UNICEF, with a combined surviving infant population of 6 million children. However, one country was required to postpone introduction to 2013 due to supply availability.
- For 2013, RV1 supply is not sufficient to meet all country introduction plans and supply constraints are contributing to delays for a number of countries.
- From 2014, the supply quantities on contracts are currently sufficient to meet the product-specific requirements of all the countries approved for RV introduction. However, as 90% of the demand is dependent on one supplier, security of supply is of concern and close planning with countries is required.
- For those countries that apply in future GAVI application rounds, including the one closing 15th September 2013, any introduction plans of RV1 may need to be postponed to 2015, at the earliest, should they choose this product presentation. Options to switch vaccine product to RV1

[8] Vaccine Vial Monitor: A thermo-sensitive indicator label placed on vaccine vial labels visually indicating the level of heat exposure and related vaccine potency.
[9] WHO, *Rotavirus: 1 Dose Tube*, WHO, Geneva, 2013 at http://www.who.int/immunization_standards/vaccine_quality/PQ_167_Rotavirus_MSD_1_dose_tube/en/index.html.

are also not supported at this time. RV5 is however available to support early introduction in country programmes.

5. Steps Forward

- UNICEF and GAVI continue to monitor closely the supply capacity through 2016 and beyond. Decisions to make incremental awards will be guided by the confirmation of new demand and the availability of supply.
- For RV5, additional supply is readily available. Country consultations continue to ensure that this option is considered as an alternative to accelerate introduction.
- UNICEF and GAVI will continue to closely monitor the development of demand, which evolves with country readiness to introduce and country progress on achieving coverage targets.
- UNICEF and GAVI will continue the close collaboration with current suppliers to improve the balance in supply and demand. The process will include oversight of annual projections and increased flexibility in response to uncertainties in the early stages of introduction.
- UNICEF continues to monitor the development of new products in the pipeline and to track the future availability of vaccines, including from new suppliers.

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