

Gavi-supported Rotavirus vaccines profiles to support country decision making

Pneumococcal and Rotavirus Working Group
Gavi Secretariat and partners, March 2019



This resource is complementary to Gavi's **Detailed Product Profiles (DPPs) for WHO prequalified vaccines** <https://www.gavi.org/about/market-shaping/detailed-product-profiles/>

The primary objective of the Detailed Product Profiles (DPPs) is to provide countries with easy access to up-to-date and comprehensive information on Gavi-supported vaccines. Countries are encouraged to consider factors beyond procurement cost and impact on country co-financing requirements: the DPPs include information on vaccine presentations, pricing, indicative wastage rates, manufacturers, cold chain volume and handling. This information will help countries decide which vaccine presentation is the best 'fit' for inclusion in their immunisation programme. Selecting a vaccine that is the most programmatically favorable for a specific country's context contributes to the sustainability of an immunisation programme. The DPPs are referenced in the 2018 New Vaccine Support guidelines and available on the Gavi website.

The secondary objective of the DPPs is to provide an overview of all WHO prequalified (WHO PQ) vaccine products. The format of the DPPs was created specifically to allow countries to compare WHO PQ vaccine products, fully informing them of their options.

Information contained in the DPPs comes from a variety of sources including the Gavi Secretariat, WHO PQ vaccine webpages, WHO position papers and UNICEF's product menu for vaccines supplied by UNICEF for Gavi-supported programmes. The Gavi Secretariat will ensure the information in the DPPs is kept up-to-date as new products become WHO pre-qualified and are available to receive Gavi-support. The DPPs will be updated on a fixed schedule (approximately every 6 months) or with more frequency if required.

THE INFORMATION CONTAINED IN THESE SLIDES AND THE DPPs IS CURRENT AS OF FEBRUARY 2019.
Please send comments or questions on the DPPs to dpp@gavi.org

Additional resources relevant for assessing vaccines and presentations:

- **Guidelines on Reporting and Renewal of Gavi support**
- **WHO position paper** <https://www.who.int/immunization/documents/positionpapers/en/>

Select criteria to assess rotavirus vaccines

(relevance of criteria may vary by country)

1. Availability

1. WHO prequalified rotavirus vaccines supported by Gavi

2. Efficacy, effectiveness, safety

3. Cost (direct)

1. Waste-adjusted price per dose / per fully immunised child
2. Co-financing amount
3. Sustainability (long term agreements on price and availability)
4. Cost-effectiveness

4. Storage and transport

1. Cold chain requirements and implications

5. Programmatic administration considerations

1. Administration route
2. Number of doses per fully immunized child
3. Risk of incorrect preparation (number of devices, number of preparation steps)
4. Risk of incorrect delivery (need for dose measurement, larger dose quantity)
5. Alignment of doses with existing routine schedule

WHO prequalified (or expected to be prequalified) rotavirus vaccines supported by Gavi

Trade name	Rotarix¹	Rotarix¹	Rotavac	Rotavac	Rotavac 5D	Rotavac 5D	Rotasiil	Rotasiil	Rotasiil
Type	Rotavirus (live, attenuated)								
Manufacturer	GSK	GSK	Bharat Biotech	Bharat Biotech	Bharat Biotech	Bharat Biotech	Serum Institute	Serum Institute	Serum Institute
NRA	Belgium	Belgium	India	India	India	India	India	India	India
Presentation*	Plastic tube	Plastic tube, in strip of tubes	Vial	Vial	Vial	Vial	Two vial set	Two vial set	Plastic tube, in strip of tubes
Form	Liquid	Liquid	Liquid (frozen)	Liquid (frozen)	Liquid	Liquid	Lyophilised	Lyophilised	Liquid
WHO PQ decision	2009	2019	2018	2018	Expected in Q1 2020	Expected in Q1 2020	2018	2018	Expected in Q2 2020
Doses in each presentation unit	1	1	5	10	1	5	1	2	1

¹The presentations of Rotarix in *plastic tube* or in *'plastic tube, in strip of tubes'* are considered similar. A switch from Rotarix in plastic tube to Rotarix in a strip of 5 tubes will not receive a switch grant.







Availability of rotavirus vaccines supported by Gavi

Trade name	Presentation	Availability for Gavi countries
Rotarix ¹	RV1, 1 dose/plastic tube, liquid	Available for <u>ongoing</u> routine vaccination in 2019. Available for new introductions from January 2020
	RV1, 1 dose/plastic tube, liquid (multi-monodose presentation with 5 single tubes connected by a bar)	Limited availability from Q4 2019 onwards.
Rotavac	RV1, 5 doses/vial, frozen	Available
	RV1, 10 doses/vial, frozen	
Rotavac 5D	RV1, 1 dose/vial, liquid	Not yet WHO prequalified. Potentially available in 2020.
	RV1, 5 doses/vial, liquid	
Rotasiil	RV5, 1 dose/vial, lyophilised	Available
	RV5, 2 doses/vial, lyophilised	
	RV5, 1 dose/plastic tube, liquid (strip of 5 tubes)	Not yet WHO prequalified. Potentially available in 2020.

¹The presentations of Rotarix in plastic tube or in plastic tube 'multi-mono' are considered similar. A switch from Rotarix in plastic tube to Rotarix in multi-mono plastic tube will not receive a Gavi switch grant.

WHO Prequalified Rotavirus vaccines supported by Gavi

Available in 2019


Trade name	Rotarix	Rotarix	Rotavac	Rotavac	Rotasiil	Rotasiil
Prese- ntation*	Plastic tube	Plastic tube, in strip of tubes	Vial	Vial	Two vial set	Two vial set
Form	Liquid	Liquid	Liquid (frozen)	Liquid (frozen)	Lyophilised	Lyophilised
Doses in each unit	1	1	5	10	1	2
Picture						

*abbreviated description. For full description, please refer to the [Detailed Product Profiles](#)

Source: https://extranet.who.int/gavi/PQ_Web/Default.aspx?nav=2

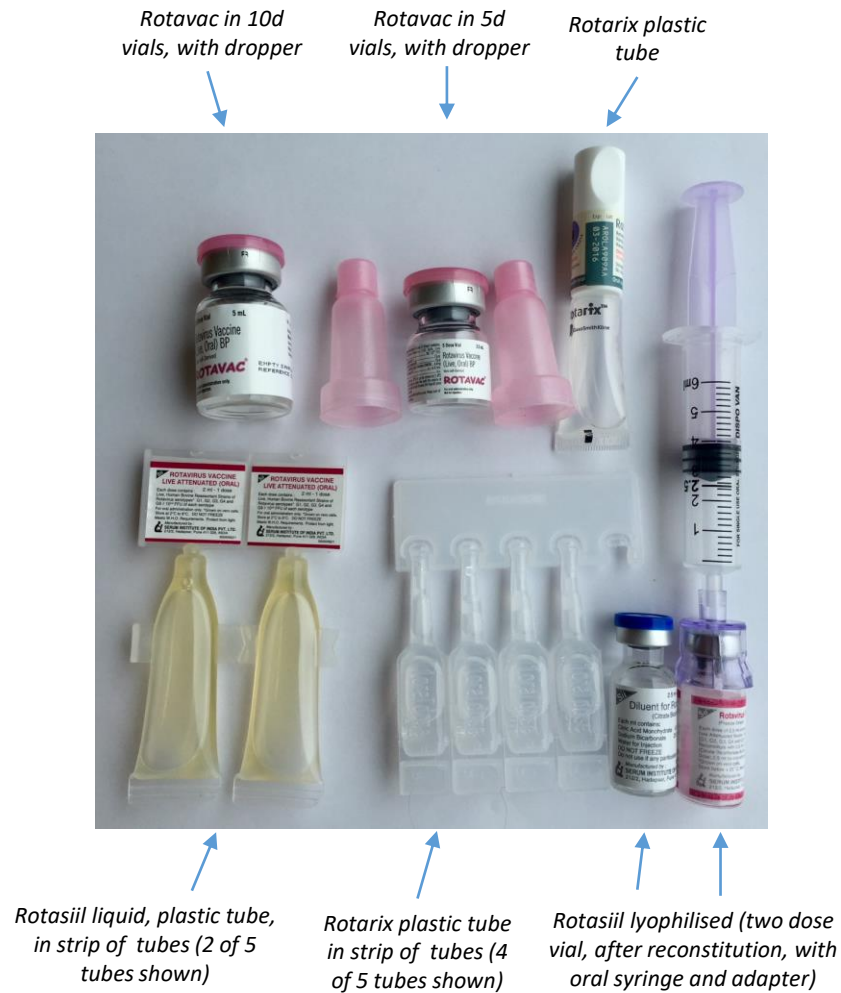
Rotavirus vaccines supported by Gavi and expected to be WHO Prequalified

New options expected to be available in 2020
(in addition to vaccines available in 2019)

Trade name	Rotavac 5D	Rotavac 5D	Rotasiil
Presentation*	Vial	Vial	Plastic tube, in strip of tubes
Form	Liquid	Liquid	Liquid
Doses in each unit	1	5	1
Picture	No picture available	No picture available	

For size comparison

(the picture below shows 6 out of 9 presentations and will be updated as soon as more samples will be received by Gavi)



Vaccine efficacy, effectiveness and safety

Summary of Key Characteristics of Currently WHO-Pre-qualified Rotavirus Vaccines

Characteristics	<i>Rotarix (RV1; GSK)</i>	<i>Rotateq (RV5; Merck)</i>	<i>Rotavac (RV1; Bharat)</i>	<i>Rotasiil (RV5; Serum Institute)</i>
Pooled effectiveness or efficacy for preventing severe rotavirus disease	Both efficacy and effectiveness data available, from multiple countries and multiple regions. Effectiveness data are shown below by country mortality profile. ¹		Only efficacy data are available, and from one country - India	Only efficacy data are available, and from two countries - India and Niger
	Low mortality	82% (95% CI, 72%-88%)	Low mortality	88% (95% CI, 83%-91%)
	Medium mortality	66% (95% CI, 51%-77%)		
	High mortality	58% (95% CI, 51%-65%)	High mortality	49% (95% CI, 40%-57%)
	Vaccine policymakers recognize differences in the vaccines' compositions and schedules but, overall, generally regard these vaccines as similar in performance			India: 37% (95% CI= 17 -51%) ³ Final analysis = 39.5% Niger: 67% (95% CI= 50 -78%) ⁴
Study sites	Multiple countries at different income and mortality levels.	Multiple countries at different income and mortality levels.	3 sites in India	6 sites in India and one site in Africa (Niger)
Date of WHO prequalification	March 2009	October 2008	January 2018	September 2018
Safety	WHO has concluded that the benefits of rotavirus vaccination against severe diarrhoea and death from rotavirus infection far exceed the risk of intussusception. ⁵		Intussusception risk in vaccinated group was not higher than in placebo group	Intussusception risk in vaccinated group was not higher than in placebo group
Mixed schedules & interchangeability of different products	<ul style="list-style-type: none"> Whenever possible, WHO recommends that the same vaccine product should be used to complete the infant vaccination series; <ul style="list-style-type: none"> If a series cannot be completed with the same type of vaccine, the available rotavirus vaccine product should be used; Restarting a series is not recommended; No published data yet exist on performance of any mixed vaccine courses that include <i>Rotavac</i> or <i>Rotasiil</i>; <ul style="list-style-type: none"> The published safety and efficacy data on mixed schedules or interchangeability that exist for <i>Rotarix</i> and <i>Rotateq</i> are reassuring;^{6,7} 			
References:				
¹ Jonesteller CL. Et al. <i>Clin Infect Dis</i> . 2017		⁵ Report of the WHO Global Advisory Committee on Vaccine Safety, 6-7 December 2017; http://apps.who.int/iris/bitstream/handle/10665/259874/WER9303.pdf?sequence=1		
² Bhandari N, et al., <i>Lancet</i> 2014		⁶ Libster R, et al. <i>Pediatrics</i> 2016.		
³ Kulkarni PS, et al., <i>Vaccine</i> 2017		⁷ Daniel C. Payne, 2018: Oral presentation at the 13 th Rotavirus Symposium, Belarus, 2018;		
⁴ Isanaka S, et al., <i>NEJM</i> 2017				

Vaccine cost (direct)

The cost estimated below is estimated based on *indicative* wastage rates.

Prices include the cost of devices.

The country specific waste-adjusted cost will vary depending on the country's own wastage rate for each presentation.

<i>Trade name</i>	Rotarix	Rotarix	Rotavac	Rotavac	Rotavac 5D	Rotavac 5D	Rotasiil	Rotasiil	Rotasiil
<i>Form</i>	Liquid	Liquid	Liquid (frozen)	Liquid (frozen)	Liquid	Liquid	Lyophilised	Lyophilised	Liquid
<i>Presentation</i>	Plastic tube	Plastic tube, in strip of tubes	Vial	Vial	Vial	Vial	Two vial set	Two vial set	Plastic tube, in strip of tubes
<i>Doses in each unit</i>	1	1	5	10	1	5	1	2	1
<i>2019-21 price per dose (USD/EUR*)</i>	\$2.29	\$2.29	\$0.85	\$0.85	\$1.58**	\$1.14**	\$1.55**	\$0.95	\$1.55**
<i>Doses per fully immunised person</i>	2	2	3	3	3	3	3	3	3
<i>2020 price per fully immunised person (USD)</i>	\$4.58	\$4.58	\$2.55	\$2.55	\$4.74	\$3.42	\$4.65	\$2.85	\$4.65
<i>Indicative wastage rate</i>	5%	5%	30%	50%	5%	10%	5%	10%	5%
<i>2020 waste-adjusted price per fully immunised person (USD)</i>	\$4.82	\$4,82	\$3.64	\$5.10	\$4.99	\$3.80	\$4.89	\$3.17	\$4.89

*The price in US dollars reflects conversion at a currency exchange rate of 1.218 USD/EUR, which reflects an average across a 5-year period (Bloomberg projected foreign exchange rates). The actual exchange rate that will be utilised to calculate the USD price at the moment of the transaction may vary.

** Final price to be confirmed after signature of Long Term Agreement between UNICEF SD and the manufacturers

Cost and co-financing implications of switch options

Gavi estimates, to be confirmed country by country. May vary after year 1 of implementation if waste rates vary.

Switch option	Programmatic changes that impact cost ³	Drivers of direct financial cost	Estimated impact on financial cost of vaccine co-financing ¹ :	
			Country in initial self-financing	Country in transition, or fully self-financing
Rotarix > Rotavac frozen in 5 doses/vial	<ul style="list-style-type: none"> • Need for more freezer capacity • Less need for refrigerated capacity 	<ul style="list-style-type: none"> + 25% wastage (from 5% to 30% in year 1) - 63% price per dose (from 2.29 to 0.85\$) + 30% doses per fully vaccinated child (from 2 to 3) 	Likely more costly	Likely less costly
Rotarix > Rotavac frozen in 10 doses/vial	<ul style="list-style-type: none"> • Need for more freezer capacity • Less need for refrigerated capacity 	<ul style="list-style-type: none"> + 45% wastage (from 5% to 50% in year 1) - 63% price per dose (from 2.29 to 0.85\$) + 30% doses per fully vaccinated child (from 2 to 3) 	Likely more costly	Marginal difference
Rotarix > Rotasil lyophilised in 1 dose /vial ²	<ul style="list-style-type: none"> • Need for more refrigerated capacity • Increased administration complexity⁴ 	<ul style="list-style-type: none"> - 32 % price per dose (from 2.29 to 1.55\$) + 30% doses per fully vaccinated child (from 2 to 3) 	No difference	Marginal difference
Rotarix > Rotasil lyophilised in 2 doses/vial	<ul style="list-style-type: none"> • Similar refrigerated capacity needs • Increased administration complexity⁴ 	<ul style="list-style-type: none"> + 5% wastage (from 5% to 10% in year 1) - 59 % price per dose (from 2.29 to 0.95\$) + 30% doses per fully vaccinated child (from 2 to 3) 	Marginal difference	Likely less costly
Rotarix > Rotavac 5D liquid in single dose/vial ²	<ul style="list-style-type: none"> • Need for more refrigerated capacity 	<ul style="list-style-type: none"> - 31% price per dose (from 2.29 to 1.58\$) + 30% doses per fully vaccinated child (from 2 to 3) 	Marginal difference	Marginal difference
Rotarix > Rotavac 5D liquid in 5 doses/vial ²	<ul style="list-style-type: none"> • Less need for refrigerated capacity 	<ul style="list-style-type: none"> + 5% wastage (from 5% to 10% in year 1) - 50% price per dose (from 2.29 to 1.14\$) + 30% doses per fully vaccinated child (from 2 to 3) 	Marginal difference	Likely less costly
Rotarix > Rotasil liquid in plastic tube strip of 5 single doses ²	<ul style="list-style-type: none"> • Need for more refrigerated capacity 	<ul style="list-style-type: none"> - 32% price per dose (from 2.29 to 1.55\$) + 30% doses per fully vaccinated child (from 2 to 3) 	No difference	Marginal difference

¹ assuming fully vaccinated children (lower coverage rates would result in lower cost).

² final price to be confirmed after signature of Long Term Agreement between UNICEF SD and the manufacturers

³ assuming fully vaccinated children

⁴ see details on slide 15

This table shows the switch options that are currently applicable to all Gavi countries with ongoing rotavirus vaccination, except two countries. More switch options will be displayed in future editions.

Rota manufacturers' pricing commitments for transitioned countries

Vaccine	Manufacturer	Commitment Duration	Summary of Conditions
Rotarix	GSK	10 years*	Country introduced with Gavi support*** Country already using GSK product May procure through UNICEF/PAHO Price freeze (=price paid during last year of support)
Rotasiil	SII	-	No price commitments
Rotavac	Bharat	-	No price commitments

Manufacturer pricing commitments are 'public announcements' made during the last Gavi replenishment, they are not legally binding.

This information is meant for the convenience and benefit of countries and should not give a false sense of assurance that Gavi is "guaranteeing" prices, and that prices are determined for every single product and country.

* From date of transition to fully self-financing, where the country receives no Gavi support

*** Gavi support = country and Gavi co-financing

Vaccine cost-effectiveness

- “Irrespective of the vaccine used, vaccination against rotavirus disease was found to be cost effective.” ([WHO position paper on Rotavirus vaccination](#))
- A recent analysis* demonstrates that the use of **ROTARIX**, **ROTAVAC**, or **ROTASIIL** would be highly cost-effective relative to no rotavirus vaccination in Bangladesh, Ghana, and Malawi.
<https://www.sciencedirect.com/science/article/pii/S0264410X18314531?via%3Dihub>
 - While ROTARIX was found to be the least costly and most cost-effective product in the three countries analyzed, the differences were small and subject to change with minor adjustments to uncertain input variables (esp. *incremental health system cost per dose*).
 - A similar analysis examining non-Gavi countries paying higher vaccine prices would likely highlight additional economic benefits of the new vaccines.

Links to the original analyses that this reanalysis is based on:

- Bangladesh: <https://www.ncbi.nlm.nih.gov/pubmed/28623028>
- Ghana: <https://www.ncbi.nlm.nih.gov/pubmed/29223486>
- Malawi: <https://www.ncbi.nlm.nih.gov/pubmed/27059360>
- Analysis of **ROTAVAC**
 - India: <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0187446>
 - Multi dose vials cost effectiveness : <https://www.ncbi.nlm.nih.gov/pubmed/21439313>
 - Multi dose vials cost effectiveness : <https://www.ncbi.nlm.nih.gov/pubmed/20566395>
- Analysis of **Rotarix/RotaTaq**
 - Afghanistan: <https://doi.org/10.1016/j.vaccine.2017.10.058>
 - Pakistan: <https://www.sciencedirect.com/science/article/pii/S0264410X18301725>
 - Senegal: <https://www.ncbi.nlm.nih.gov/pubmed/25919151>
 - Kenya and Uganda: <https://www.ncbi.nlm.nih.gov/pubmed/25919149>

*Pecenka C, Debellut F, Bar-Zeev N, et al. Re-evaluating the cost and cost-effectiveness of rotavirus vaccination in Bangladesh, Ghana, and Malawi: A comparison of three rotavirus vaccines. *Vaccine*. 2018;36(49):7472-7478.

Storage and transport

(shelf life, VVM, volume per fully immunised person)

Trade name	Rotarix	Rotarix	Rotavac	Rotavac	Rotavac 5D	Rotavac 5D	Rotasiil	Rotasiil	Rotasiil
Presentation	1 dose/plastic tube, liquid	1 dose/plastic tube, liquid in strip of tubes	5 doses/vial, frozen	10 doses/vial, frozen	1 dose/vial, liquid	5 doses/vial, liquid	1 dose/vial, lyophilised	2 doses/vial, lyophilised	1 dose/plastic tube, liquid (strip of 5 tubes)
Shelf-life¹	24 months at 2 - 8 °C	24 months at 2 - 8 °C	60 months at -20 °C, 6 months at 2-8 °C post thaw	60 months at -20 °C, 6 months at 2-8 °C post thaw	24 months at 2-8°C	24 months at 2-8°C	30 months at 2-8 °C	30 months at 2-8 °C	24 months at 2-8 °C
Cold chain volume per fully immunised person (cm³)¹	In cartons of 50 doses: 34.2 cm ³	In cartons of 50 doses: 23.6 cm ³	12.6 cm ³	9.6 cm ³	48 cm ³	12.6 cm ³	52.7 cm ³ , with diluent stored at ambient temperature 105.5 cm ³ , with diluent stored in the cold chain	31.6 cm ³ , with diluent stored at ambient temperature 63.3 cm ³ , with diluent stored in the cold chain	75.72cm ³
Wastage adjusted cold chain volume per fully immunised person (cm³)^{1 5}	36.0 cm ³	24.8 cm ³	18 cm ³	19.2 cm ³	50.5 cm ³	14 cm ³	55.5 cm ³ , with diluent stored at ambient temperature 111.0 cm ³ , with diluent stored in the cold chain	35.2 cm ³ , with diluent stored at ambient temperature 70.3 cm ³ , with diluent stored in the cold chain	79.7cm ³
Vaccine vial monitor type¹	Type 7	Type 7	Type 2	Type 2	Type 7	Type 7	Type 30	Type 30	Type 7
Handling open vials¹	n/a	n/a	Opened vials of this vaccine should be discarded 6 hours after opening or at the end of the immunization session, whichever comes first.		n/a	Opened vials should be discarded 6 hours after opening or at the end of the immunization session, whichever comes first.	n/a	Opened vials should be discarded 6 hours after opening or at the end of the immunization session, whichever comes first.	n/a
Remarks WHO¹	n/a	n/a	Can be stored at 2-8°C until discard point of VVM2. (at 5°C, the VVM2 discard point is 225 days). For the delivery to PAHO, without VVM, a maximum storage of 6 months at 2-8°C		TBD	TBD	n/a	n/a	TBD
Notes	n/a	n/a	ROTAVAC® can be subjected to 6 freeze- thaw cycles		TBD	TBD	The shelf-life of diluent is 60 months at 2 to 8°C. The diluent should not be frozen.		TBD

1 Source: WHO PQ webpage: WHO updates these webpages as new information on products becomes available. Please refer to these pages (WHO PQ link) for the most up-to-date information. For presentations not yet WHO prequalified, data is based on discussions with manufacturers and partners in 2017.

5 Source: Review of WHO indicative vaccine wastage rate assumptions, 2017

Cold Chain implications for Rotavac (Gavi Analysis)

	Central level	Sub-national level (region/ province/store)	District/ health zone/ LGA stores	Service delivery level
Storage	<p>Store at negative temperatures (freezer or freezer room)</p> <p>If freezer capacity is insufficient:</p> <ul style="list-style-type: none"> • countries could move lyophilized vaccines from the freezer rooms to the cold rooms (refrigerators) to make space • countries may procure a couple of freezers if the quantity is not superior to 5 (for which a small freezer room may be more efficient) 	<p>Store at negative temperatures (freezer or freezer room)</p> <ul style="list-style-type: none"> • All countries have freezers that are used for storing polio vaccines and/or ice packs • Countries may decide to procure a small freezer room which could be used for storing this vaccine and others 	<p>If liquid: store in refrigerators</p> <p>If frozen: store in freezers</p> <ul style="list-style-type: none"> • Storing in refrigerators is fine if the district collects vaccines on a monthly basis 	<p>Store in refrigerators</p>
Distribution to the next level	<p>Transport in negative temperatures</p> <ul style="list-style-type: none"> • Transport in cold boxes with fully frozen ice packs (same for refrigerated truck (2-8C) or normal truck) 	<p>Different options based upon country stock turnover rates:</p> <ul style="list-style-type: none"> • Transport refrigerated as liquid, which will kick start the 6 months potency threshold • Transport at negative temperatures (cold boxes with fully frozen ice packs) (encouraged) 	<p>Transport refrigerated as liquid</p>	
Gavi support (as an example)	<ul style="list-style-type: none"> • Cold boxes • Freezers 	<ul style="list-style-type: none"> • cold boxes • small freezer room 	<ul style="list-style-type: none"> • freezers 	<ul style="list-style-type: none"> • Refrigerators (optional)

*countries may request support to procure the items reflecting them in the budget of either VIG / switch grant /CCEOP/ HSS flexibilities

Programmatic administration considerations

(risks of incorrect preparation or incorrect delivery)

	Rotarix	Rotarix (in strip of 5 tubes)	Rotavac (in 5 or 10 dose vials)	Rotasiil (in single or 2 dose vials)	Rotavac 5D	Rotavac 5D	Rotasiil (in strip of 5 tubes)
Route	Oral	Oral	Oral	Oral	Oral	Oral	Oral
Form	Liquid	Liquid	Liquid (frozen)	Lyophilised	Liquid*	Liquid*	Liquid*
Doses per fully immunised child	2	2	3	3	3	3	3
Dose quantity	1.5 ml	1.5 ml	0.5 ml (5 drops)	2.5 ml	0.5ml (5 drops)	0.5ml (5 drops)	2ml
Devices per unit	1	1 (multi-monodose presentation with 5 single tubes connected by a bar)	2 (vial and dropper)	4 (single dose) 5 (2 dose vial) Diluent vial, vaccine vial, adapter, syringe for reconstitution and for oral administration	2 (vial and dropper)	2 (vial and dropper)	1 (5 single-dose tubes attached by a strip)
Preparation steps (see WHO training slides for details)	1	1	4	8	1	1	1
Need for dose measurement	No	No	Yes	Yes	No	Yes	No

*Liquid presentation expected to be available in 2020

Key references

WHO [Prequalification](https://www.who.int/immunization/diseases/rotavirus/en/) information: <https://www.who.int/immunization/diseases/rotavirus/en/>

UNICEF [rotavirus market note](#) (Nov 2018)

Gavi [Detailed Product Profiles](#)

WHO training materials: <https://www.who.int/immunization/diseases/rotavirus/en/>