Available & New Rotavirus Vaccines

Umesh D. Parashar
Chief, Viral Gastroenteritis Branch
CDC, Atlanta, USA
Special thanks for slides
RotaTeq & Rotarix licensed in 2006

<table>
<thead>
<tr>
<th>RotaTeq™ (Merck&amp;Co., Inc.)</th>
<th>Rotarix™ (GlaxoSmithKline)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 oral doses beginning at 6 weeks</td>
<td>2 oral doses beginning at 6 weeks</td>
</tr>
</tbody>
</table>
WHO Recommends Global Use of Rotavirus Vaccines
Decision Could Help Protect Millions of Children in Africa and Asia from Lethal Diarrheal Disease
98 countries have implemented rotavirus vaccination programs
Vaccine impact data available from all world regions and income groups

Belgium: A major hospital saw a decline in the percent of hospitalized diarrhea due to rotavirus in <5s of 66% by the 3rd year following vaccine introduction.

Moldova: Rotavirus hospitalizations in 2 national hospitals fell 73% in infants by the 2nd year following vaccine introduction.

U.S.: The lab diagnosis of rotavirus declined 58-90% since rotavirus vaccines were introduced in 2006.

Brazil: Diarrheal deaths in children <5 were cut by more than half (55%) during four years following vaccine introduction & diarrheal hospitalizations by 36%.

Mexico: Deaths due to diarrhea in <5s fell 53% on average in post-vaccination years, preventing nearly 1,000 deaths/year.

Rwanda: With 99% vaccination coverage, hospital admissions due to rotavirus fell 61-70% in <5s in 2 years post vaccine introduction.

Malawi: Vaccination was 71% effective in preventing rotavirus-related hospitalizations in the first year of life.

Thailand: In a pilot introduction of rotavirus vaccine in 1 province, hospitalizations from rotavirus declined 88% over 2 years.
What are the remaining challenges to global rotavirus vaccine introduction?
Rotavirus remains the leading cause of severe diarrhea in developing countries after rotavirus vaccine introduction.

Before vaccine:
- Rotavirus: 55%
- Norovirus: 5%
- ETEC: 6%
- Cryptosporidium: 6%
- Other: 28%

Plats Mills et al JID 2017
Countries will transition from GAVI eligibility for vaccine subsidy support

Cost effectiveness of the vaccines are going to become more and more crucial - vaccine efficacy and costs of vaccine & vaccine delivery
Rotavirus vaccine introductions are affected by global supply shortfall

More than 90 million children lack access to these life-saving vaccines.

Gavi country introductions

2018: Afghanistan, Uganda, Bangladesh, Benin, DRC, Nepal (all delayed due to supply issue)
2019: Bhutan, CAR, Kyrgyz Rep, Lao PDR, Nigeria, Solomon Islands, Sri Lanka
2020: Indonesia, Myanmar, Timor-Leste, Ukraine
2021: Azerbaijan, Korea DPR, Mongolia, Vietnam
2022: Chad Comoros, Guinea

Merck Pulls Out Of Agreement To Supply Life-Saving Vaccine To Millions Of Kids

The pharmaceutical giant will stop delivering its rotavirus vaccine to four West African countries and will begin to sell it in China for likely more than 10 times the cost.
Prime Minister Modi

“Government of India will provide a rotavirus vaccine to all Indian children”

Two Indian-made rotavirus vaccines licensed in 2018
Rotavirus vaccine in NIP - Current and Proposed scale up by moHFW

- **RVV States (9 States)**
- **RVV States in 2018 (2 states)**

- RVV scale up in 2016-2018 (11 States)
- RVV scale up NNM in 2018 (3 NNM States)
- RVV scale up NNM in 2019 (9 NNM States)
- RVV scale up NNM in 2020 (Remaining states)
Rotavac and RotaSIIL were pre-qualified by WHO in 2018

**ROTAVAC™, Bharat Biotech**
(derived from a single Indian neonatal strain of human rotavirus) G9P11

**RotaSIIL™, Serum Institute**
(Reassorted bovine-human rotavirus)
Genetically engineered vaccine consisting of 5 different strains to protect against the 5 most common human rotaviruses G1,2,3,4 & 9
Efficacy of Indian rotavirus vaccines is comparable to multi-national vaccines

Efficacy against severe disease in first year of life

Oral vaccine pipeline

- **Live-attenuated, oral (WHO PQ):**
  - Liquid BRV BUTANTAN Brazil
  - Liquid BRV WUHAN China
  - Liquid presentation Bharat Biotech
  - RV3-BB Biofarma, Indonesia
  - Heat stable pentavalent Hilleman MSD, India
  - Dormant
  - National license
  - WHO PQ

- **Live-attenuated, oral**
  - ROTARIX GSK
  - ROTATEQ Merck
  - ROTAVAC Bharat Biotech
  - ROTASIIIL Serum Institute

**Neonatal schedule**
Non-replicating rotavirus vaccines

Safety and immunogenicity of a parenteral P2-VP8-P[8] subunit rotavirus vaccine in toddlers and infants in South Africa: a randomised, double-blind, placebo-controlled trial

Michelle J Groome, Anthonet Koen, Alan Fox, Nicola Page, Lisa Jose, Shabir A Madhi, Monica McNeal, Len Dally, Ik Sung Cho, Maureen Power, Jorge Flores, Stanley Cryz

Vaccine 36 (2018) 2233–2236

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Short communication

The future control of rotavirus disease: Can live oral vaccines alone solve the rotavirus problem? ∗

Roger L. Glass a,b,c, Baoming Jiang b, Umesh Parashar b

a Fogarty International Center, National Institutes of Health, Bethesda, MD, USA
b Viral Gastroenteritis Branch (previously), Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA
### Achieving rotavirus introduction and impact in developing countries

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insufficient global supply</td>
<td>Support existing suppliers</td>
</tr>
<tr>
<td>Vaccine cost</td>
<td>Support new suppliers</td>
</tr>
<tr>
<td>Large cold-chain footprint</td>
<td>Ensure second generation and new rotavirus vaccines have acceptable presentation</td>
</tr>
<tr>
<td>Efficacy in low income countries half that observed in high income countries</td>
<td>Pursue next generation rotavirus vaccines (i.e., parenteral, adjuvanted) to improve efficacy</td>
</tr>
</tbody>
</table>
Key Resources
# GAVI rotavirus vaccine profiles

<table>
<thead>
<tr>
<th>Attribute</th>
<th>GSK (Rotarix)</th>
<th>Merck (RotaTeq)</th>
<th>BBIL (ROTAVAC)</th>
<th>SIIL (ROTASIIIL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presentation</td>
<td>Liquid (1 dose plastic tube)</td>
<td>Liquid (1 dose plastic tube)</td>
<td>Liquid (frozen) (1, 5 or 10 dose vial)</td>
<td>Lyophilized (1 or 2 dose vial)</td>
</tr>
<tr>
<td>Doses/Course</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Price/Course</td>
<td>$5.00</td>
<td>$10.50</td>
<td>$3.00</td>
<td>~$4.80</td>
</tr>
<tr>
<td>Volume/Course</td>
<td>34 cm$^3$</td>
<td>139 cm$^3$</td>
<td>94.8 cm$^3$/28.2 cm$^3$ /11.7 cm$^3$</td>
<td>105.5 cm$^3$ /63.3 cm$^3$ (Including diluent)</td>
</tr>
<tr>
<td>VVM</td>
<td>7</td>
<td>None</td>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>PQ date</td>
<td>2008</td>
<td>2008</td>
<td>2018</td>
<td>2018</td>
</tr>
</tbody>
</table>

[link to GAVI vaccine profiles](https://www.gavi.org/library/gavi-documents/supply-procurement/rotavirus-vaccine-profiles/)
### UNICEF vaccine product menu

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Form</th>
<th>Presentation</th>
<th>Number of awarded manufacturing</th>
<th>Storage space (Number/Liter)</th>
<th>VVM</th>
<th>Product availability 2019</th>
<th>Product availability 2020</th>
<th>Product availability 2021</th>
<th>Product availability 2022</th>
<th>Projected Weighted Average Price per Dose 2019</th>
<th>Projected Weighted Average Price per Dose 2020</th>
<th>Projected Weighted Average Price per Dose 2021</th>
<th>Projected Weighted Average Price per Dose 2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTP-HepB-Hib</td>
<td>Liquid</td>
<td>1 ds</td>
<td>6</td>
<td>10.3 - 16.8</td>
<td>VVM14</td>
<td>Yes</td>
<td>Supply on demand</td>
<td>Supply on demand</td>
<td>Supply on demand</td>
<td>$1.16</td>
<td>Pending tender</td>
<td>Pending tender</td>
<td>Pending tender</td>
</tr>
<tr>
<td>DTP-HepB-Hib</td>
<td>Liquid</td>
<td>10 ds</td>
<td>4</td>
<td>2.1 - 4.4</td>
<td>VVM14</td>
<td>Yes</td>
<td>Supply on demand</td>
<td>Supply on demand</td>
<td>Supply on demand</td>
<td>$0.70</td>
<td>Pending tender</td>
<td>Pending tender</td>
<td>Pending tender</td>
</tr>
<tr>
<td>HPV4</td>
<td>Liquid</td>
<td>1 ds</td>
<td>1</td>
<td>15.0</td>
<td>VVM30</td>
<td>Yes</td>
<td>Limited supply</td>
<td>Limited supply</td>
<td>Limited supply</td>
<td>$4.50</td>
<td>Pending tender</td>
<td>Pending tender</td>
<td>Pending tender</td>
</tr>
<tr>
<td>HPV2</td>
<td>Liquid</td>
<td>2 ds</td>
<td>1</td>
<td>4.8</td>
<td>VVM30</td>
<td>Yes</td>
<td>Limited supply</td>
<td>Limited supply</td>
<td>Limited supply</td>
<td>$4.60</td>
<td>Pending tender</td>
<td>Pending tender</td>
<td>Pending tender</td>
</tr>
<tr>
<td>IPV</td>
<td>Liquid</td>
<td>1 ds</td>
<td>1</td>
<td>16.7</td>
<td>VVM7</td>
<td>Yes</td>
<td>Limited supply</td>
<td>Limited supply</td>
<td>Limited supply</td>
<td>$3.50</td>
<td>$2.99</td>
<td>$2.99</td>
<td>$2.99</td>
</tr>
<tr>
<td>IPV</td>
<td>Liquid</td>
<td>5 ds</td>
<td>2</td>
<td>4 - 8.7</td>
<td>VVM7</td>
<td>Yes</td>
<td>Limited supply</td>
<td>Limited supply</td>
<td>Limited supply</td>
<td>$2.67</td>
<td>$2.67</td>
<td>$2.65</td>
<td>$2.65</td>
</tr>
<tr>
<td>IFV</td>
<td>Liquid</td>
<td>10 ds</td>
<td>1</td>
<td>2.46</td>
<td>VVM7</td>
<td>Yes</td>
<td>Limited supply</td>
<td>Limited supply</td>
<td>Limited supply</td>
<td>$1.81</td>
<td>$1.81</td>
<td>$1.81</td>
<td>$1.81</td>
</tr>
<tr>
<td>Meningococcal A (Hemog)</td>
<td>Lyophilised</td>
<td>10 ds + Diluent</td>
<td>1</td>
<td>2.60</td>
<td>3.11</td>
<td>VVM30</td>
<td>Yes</td>
<td>Supply on demand</td>
<td>Supply on demand</td>
<td>$0.71</td>
<td>Pending tender</td>
<td>Pending tender</td>
<td>Pending tender</td>
</tr>
<tr>
<td>Meningococcal A (Hemog)</td>
<td>Lyophilised</td>
<td>10 ds + Diluent</td>
<td>1</td>
<td>2.10</td>
<td>3.11</td>
<td>VVM30</td>
<td>Yes</td>
<td>Supply on demand</td>
<td>Supply on demand</td>
<td>$0.60</td>
<td>Pending tender</td>
<td>Pending tender</td>
<td>Pending tender</td>
</tr>
<tr>
<td>OCV</td>
<td>Liquid</td>
<td>1 ds</td>
<td>2</td>
<td>11 - 16.8</td>
<td>VVM30</td>
<td>Yes</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>$2.00</td>
<td>Pending tender</td>
<td>Pending tender</td>
<td>Pending tender</td>
</tr>
<tr>
<td>OCV</td>
<td>Liquid</td>
<td>1 ds</td>
<td>1</td>
<td>7.80</td>
<td>VVM30</td>
<td>Yes</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>$1.24</td>
<td>Pending tender</td>
<td>Pending tender</td>
<td>Pending tender</td>
</tr>
<tr>
<td>PCV16</td>
<td>Liquid</td>
<td>2 ds</td>
<td>1</td>
<td>8.84</td>
<td>VVM30</td>
<td>Yes</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>$3.05</td>
<td>$3.05</td>
<td>$3.05</td>
<td>$3.05</td>
</tr>
<tr>
<td>PCV16</td>
<td>Liquid</td>
<td>4 ds</td>
<td>1</td>
<td>2.40</td>
<td>VVM30</td>
<td>Yes</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>$3.05</td>
<td>$3.05</td>
<td>$3.05</td>
<td>$3.05</td>
</tr>
<tr>
<td>PCV13</td>
<td>Liquid</td>
<td>1 ds</td>
<td>1</td>
<td>12.01</td>
<td>VVM30</td>
<td>Yes</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>$3.30</td>
<td>$3.30</td>
<td>$3.30</td>
<td>$3.30</td>
</tr>
<tr>
<td>PCV15</td>
<td>Liquid</td>
<td>4 ds</td>
<td>1</td>
<td>3.50</td>
<td>VVM30</td>
<td>Yes</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>$2.90</td>
<td>$2.90</td>
<td>$2.90</td>
<td>$2.90</td>
</tr>
<tr>
<td>Rota4</td>
<td>Liquid</td>
<td>1 ds</td>
<td>1</td>
<td>17.12</td>
<td>VVM14</td>
<td>Yes</td>
<td>Limited supply</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>$1.88</td>
<td>$1.88</td>
<td>$1.88</td>
<td>Pending tender</td>
</tr>
<tr>
<td>Rota5</td>
<td>Liquid</td>
<td>1 ds</td>
<td>1</td>
<td>46.25</td>
<td>-</td>
<td>No</td>
<td>Limited supply</td>
<td>No supply</td>
<td>No supply</td>
<td>$3.20</td>
<td>No supply</td>
<td>No supply</td>
<td>Pending tender</td>
</tr>
<tr>
<td>Rota9</td>
<td>Lyophilised</td>
<td>2 ds</td>
<td>1</td>
<td>10.84</td>
<td>VVM30</td>
<td>Yes</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>$0.95</td>
<td>$0.95</td>
<td>$0.95</td>
<td>Pending tender</td>
</tr>
<tr>
<td>Rota9</td>
<td>Liquid</td>
<td>5 ds</td>
<td>1</td>
<td>4.30</td>
<td>VVM2</td>
<td>Yes</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>$0.85</td>
<td>$0.85</td>
<td>$0.85</td>
<td>Pending tender</td>
</tr>
<tr>
<td>Rota11</td>
<td>Liquid</td>
<td>5 ds</td>
<td>1</td>
<td>4.30</td>
<td>VVM2</td>
<td>Yes</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>Needs planning</td>
<td>$0.85</td>
<td>$0.85</td>
<td>$0.85</td>
<td>Pending tender</td>
</tr>
</tbody>
</table>

Rotavirus Disease and Immunization: Series of Briefs (2019)

Six rotavirus-focused briefs cover epidemiology and disease burden, available vaccine products, the impact of vaccination, economic costs of rotavirus disease and the value of vaccines, safety, and introduction and coverage status. The Council’s series also includes a supplemental brief on the broad impact of early childhood diarrhea.

View the Council’s webinar launch of the briefs from 7 May, 2019.

Share the briefs using the Council’s social media toolkit.

CURRENT AND UPCOMING ROTAVIRUS VACCINES

INTRODUCTION

The rotavirus vaccine landscape, or availability of products, has recently expanded considerably and is expected to continue to do so. With the prequalification by WHO of two new vaccines produced in India, there are now four globally available rotavirus vaccines. Additional vaccines are in advanced stages of development and thus the pipeline of rotavirus vaccines will continue to grow in the coming years (see Table 1). The increase in the number of rotavirus vaccines is beneficial for several reasons. It increases the choice countries have in selecting vaccine products and presentations and helps to improve the global supply of rotavirus vaccines to meet current and future demand. The expanded number of products could help lower vaccine costs, a major barrier to introducing rotavirus vaccines in some countries. In addition, some products in development have shown higher rates of efficacy in low-income countries. This brief focuses on the currently available rotavirus vaccines and those most likely to become available in the next several years.

TABLE 1: CURRENT ROTAVIRUS VACCINES AND CANDIDATES IN ADVANCED STAGES OF DEVELOPMENT (MANUFACTURER, COUNTRY)

<table>
<thead>
<tr>
<th>WHO prequalified</th>
<th>Nationally licensed</th>
<th>In advanced stages of development</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROTARIX® (GliaSerdBiorek Biologics, Belgium)</td>
<td>Lanzhou Lamb Rotavirus (Lanzhou Institute of Biological Products, China)</td>
<td>RV3-BB (IT Biotech, South Korea)</td>
</tr>
<tr>
<td>RotaToq® (Merck &amp; Co., Inc., U.S.A.)</td>
<td>ROTAVAC® (Bharat Biotech, India)</td>
<td>LLR reassortants (Lanzhou Institute of Biological Products, China)</td>
</tr>
<tr>
<td>ROTASIL® (Bharat Biotech, India)</td>
<td>ROTAVIN-MI (POLYVAC, Vietnam)</td>
<td>Trivalent P2-VP8 (injectable subunit vaccine) (SK Bioscience, South Korea)</td>
</tr>
</tbody>
</table>