ROTASIL®
Rotavirus vaccine

by

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Introduction

- The steady increase in the number of vaccines a child receives has resulted in greater pressure on the cold chain distribution system.
- Serum Institute’s new Rotavirus vaccine - ROTASIIL® is the first vaccine in the world that can be stored at a temperature below 25°C for its shelf life of 30 months.
- This unique characteristic will help Public health professionals deliver this vaccine more easily to their target population.
- The slides that follow will acquaint you with this vaccine.

World’s First Thermo Stable Vaccine!
SII’s Rotavirus Vaccine: ROTASIIL

Master seed virus (Characterized) from Dr. Kapikian, NIH-USA

- Working seed prepared by SIIPL
- Characterized as per WHO TRS and Ph. Eur

VERO Cell substrate (CCL-81) from ATCC

- Master Cell Bank and Master working cell bank prepared by SIIPL
- Characterized as per WHO TRS and Ph. Eur
ROTASIIL®
Rotavirus Vaccine, Live Attenuated Oral, Freeze-Dried

1 dose - 2.5 ml. 2 dose – 5.0 ml

Each dose of 2.5 ml contains:
Live Attenuated Bovine-Human Rotavirus Reassortant [G1, G2, G3, G4 and G9]* ≥ 10^{5.6} FFU/Serotype.
*Grown on VERO cells

Reconstitute with Diluent for Rotavirus Vaccine

World’s First Thermo Stable Vaccine!
Diluent: Citrate Bicarbonate Buffer

- The vaccine has to be reconstituted using a diluent
- The diluent works as an antacid, serving both as a vehicle for the vaccine and neutralizing the stomach pH
- Reconstitution volume:
  - 1 dose - 2.5 ml.
  - 2 dose – 5.0 ml
- Each ml contains:
  - Citric Acid Monohydrate-9.6 mg,
  - Sodium Bicarbonate-25.6 mg,
Accessories

► One of the factors that contributed to the vaccine’s extraordinary heat stability is the Lyophilization process.

► To be able to Lyophilize the product, it is essential that the vaccine be filled in glass vials.

► Accessories for the vaccine administration are designed to ensure that the program personnel get a clear message that the product is oral.

► The syringe provided has a tip on which a needle cannot be fitted.

► The syringe is supplied with an adapter which cannot be accidentally used for injection.
No need of REFRIGERATION!

- Lyophilized Vaccine is stored at Temperatures below 25°C for 30 months.
- Reconstituted Vaccine
  If stored at a temperature between 2° to 8°C, the vaccine can be used up to 6 hours.

World’s First Thermo Stable Vaccine!
Dose Regimen

Three doses of vaccines are scheduled to be administered orally to the infants.

<table>
<thead>
<tr>
<th>Dose</th>
<th>Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Dose</td>
<td>6 weeks</td>
</tr>
<tr>
<td>2nd Dose</td>
<td>10 weeks</td>
</tr>
<tr>
<td>3rd Dose</td>
<td>14 weeks</td>
</tr>
</tbody>
</table>
• Drug Substance (Bulk vaccine) is stable more than five years if stored at -20°C.

• Drug product (Final vaccine) is stable at Below 25°C for 36 months, At 37°C and 40°C for more than six months (initial batches showed stability till 18 months)

• Reconstituted vaccine can be used within 6 hours if stored at 2 to 8°C.
ROTASIIL® is stable at below 25°C for 36 months, 37°C and 40°C for more than six months.
Bovine rotavirus pentavalent vaccine development in India

Jagdish K. Zade, Prasad S. Kulkarni *, Sajjad A. Desai, Rajendra N. Sabale, Sameer P. Naik, Rajeev M. Dhere

Serum Institute of India Ltd., Pune, India

ARTICLE INFO

Article history:

Keywords:
Bovine rotavirus pentavalent rotavirus vaccine (BRV-PV)
Serum Institute of India Ltd.
Development
Clinical trials

ABSTRACT

A bovine rotavirus pentavalent vaccine (BRV-PV) containing rotavirus human-bovine (UK) reassortant strains of serotype G1, G2, G3, G4 and G9 has been developed by the Serum Institute of India Ltd, in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID), USA. The vaccine underwent animal toxicity studies and Phase I and II studies in adults, toddlers and infants. It has been found safe and immunogenic and will undergo a large Phase III study to assess efficacy against severe rotavirus gastroenteritis.

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Three doses of BRV-PV, an oral rotavirus vaccine, had an efficacy of 66.7% against severe rotavirus gastroenteritis among infants in Niger.
Patent

**United States Patent**
Dhere et al.

**Patent No.:** US 8,795,686 B2
**Date of Patent:** Aug. 5, 2014

**Inventors:** Rajeev M. Dhere, Pune (IN); Sambhaji S. Pisal, Pune (IN); Jagdish K. Zade, Pune (IN)

**Assignee:** Serum Institute of India, Pune (IN)

**Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 493 days.

**Appl. No.:** 13/056,557
**PCT Filed:** Nov. 6, 2009

**Field of Classification Search**
None
See application file for complete search history.

**References Cited**

**U.S. PATENT DOCUMENTS**

**WO**
WO 02/09749  * 2/2002

**FOREIGN PATENT DOCUMENTS**

**OTHER PUBLICATIONS**
ROTASIIL®
Rotavirus Vaccine, Live Attenuated Oral, Freeze-Dried

Indian Clinical Trial was a collaborative effort between:

Bill & Melinda Gates Foundation
PATH
Serum Institute of India Pvt. Ltd.
Programmatic Implementation

• Production capacity expansion 100 million plus.
• Product supply to Indian government (4 million doses till December 2017)
• WHO-PQ (Dossier is submitted)
• Registration in different countries
• Supply to UNICEF and PAHO
Rotavirus Liquid Vaccine

Single Dose Presentation
Rotavirus Liquid Vaccine

Multi-Mono Dose Presentation
Why liquid formulation?

• Easy administration (ready to use format).

• Market demand for ready to use formulation.

• Meets WHO VPPAG recommendation.

• Animal Toxicity study and Phase I clinical study completed. Phase III study will be started in October 2017.

• Commercial license expected in December 2018.
• Vaccine qualifies the requirement of VVM7 (37°C for 7 days).

• Three batches were prepared for stability and the study indicated that the product is stable at
  ✓ 2-8°C for 24 months
  ✓ 25°C for 6 months
  ✓ 37°C for 1 week
Thank You