GLORIOUS 50 YEARS 1967-2017 Protection from birth onwards

ROTASIIL®

Rotavirus vaccine

by

Dr. Suresh Jadhav

Executive Director

SERUM INSTITUTE OF INDIA PVT. LTD.

Cyrus Poonawalla Group

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Lyophilized Rotavirus Vaccine

Introduction

ROTASIIL®
Rotavirus Vaccine, Live Attenuated
Oral, Freeze-Dried

- 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

ROTASIIL®
Rotavirus Vaccine, Live Attenuated
Oral, Freeze-Dried

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

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]* $\geq 10^{5.6}$ FFU/Serotype.
*Grown on VERO cells

Reconstitute with Diluent for Rotavirus Vaccine

World's First Thermo Stable Vaccine!

Diluent: Citrate Bicarbonate Buffer

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- 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

ROTASIIL®
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- 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.

3mL Oral syringe

Adapter

No need of REFRIGERATION!

ROTASIIL®
Rotavirus Vaccine, Live Attenuated
Oral, Freeze-Dried

- **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

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

Dose	Weeks
1st Dose	6 weeks
2nd Dose	10 weeks
3rd Dose	14 weeks

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Summary of Stability

- 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 2to 8°C.

Vaccine 35 (2017) 2962–2969

Contents lists available at ScienceDirect

Vaccine

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

Stability of heat stable, live attenuated Rotavirus vaccine (ROTASIIL®)

Sameer P. Naik, Jagdish K. Zade *, Rajendra N. Sabale, Sambhaji S. Pisal, Ravi Menon, Subhash G. Banl
Sunil Gairola, Rajeev M. Dhere

Serum Institute of India PVT LTD, 212/2, Hadapsar, Pune 411028, India

ROTASIIL® is stable at below 25°C for 36 months, 37°C and 40°C for more than six months.

A B S T R A C T

Vaccines currently available across the globe are stored and transported in a continuous cold-chai
8 °C or below −20 °C. A temperature excursion outside this range affects the potency of the vaccine
vaccines need to be discarded leading wastage. The Rotavirus disease burden is predominantly re
in developing and low-income countries and therefore, has entered or poised to enter their n
immunization programs. These countries already have several limitations for effective storage, n
nance and distribution of vaccines in a cold-chain and this introduction is expected to further stre
fragile ecosystem. To help mitigate the cold chain related issues, SIIPL has developed a thermostabl
virus vaccine ROTASIIL® which can be stored at a temperature below 25 °C for 36 months, complet
passing the standard 2–8 °C cold storages. In addition it has the capability to withstand temperat
37 °C and 40 °C for 18 months and short term exposure to 55 °C. It can also tolerate a temperature
of being thawed from an extreme cold temperature of −20 °C to a high temperature of 42 °C. The v
contains serotypes G1, G2, G3, G4 and G9 (UK-Bovine reassortant strains procured from National In
of Health-USA). The vaccine is recently licensed in India.

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Vaccine 32S (2014) A124–A128

Contents lists available at ScienceDirect

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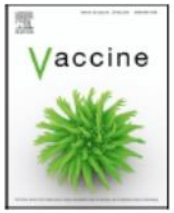
journal homepage: www.elsevier.com/locate/vaccine



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:

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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.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of a Low-Cost, Heat-Stable Oral Rotavirus Vaccine in Niger

Sheila Isanaka, Sc.D., Ousmane Guindo, M.D., Celine Langendorf, Pharm.D., M.P.H., Amadou Matar Seck, M.D., Brian D. Plikaytis, M.Sc., Nathan Sayinzoga-Makombe, M.P.H., Monica M. McNeal, M.Sc., Nicole Meyer, M.Sc., Eric Adehossi, M.D., Ali Djibo, M.D., Bruno Jochum, M.S., and Rebecca F. Grais, Ph.D.

ABSTRACT

BACKGROUND
Each year, rotavirus gastroenteritis is responsible for about 37% of deaths from diarrhea among children younger than 5 years of age worldwide, with a disproportionate effect in sub-Saharan Africa.

METHODS
We conducted a randomized, placebo-controlled trial in Niger to evaluate the efficacy of a live, oral bovine rotavirus pentavalent vaccine (BRV-PV, Serum Institute of India) to prevent severe rotavirus gastroenteritis. Healthy infants received three doses of the vaccine or placebo at 6, 10, and 14 weeks of age. Episodes of gastroenteritis were assessed through active and passive surveillance and were graded on the basis of the score on the Vesikari scale (which ranges from 0 to 20, with higher scores indicating more severe disease). The primary end point was the efficacy of three doses of vaccine as compared with placebo against a first episode of laboratory-confirmed severe rotavirus gastroenteritis (Vesikari score, ≥11) beginning 28 days after dose 3.

RESULTS
Among the 3508 infants who were included in the per-protocol efficacy analysis, there were 31 cases of severe rotavirus gastroenteritis in the vaccine group and 87 cases in the placebo group (2.14 and 6.44 cases per 100 person-years, respectively), for a vaccine efficacy of 66.7% (95% confidence interval [CI], 49.9 to 77.9). Similar efficacy was seen in the intention-to-treat analyses, which showed a vaccine efficacy of 69.1% (95% CI, 55.0 to 78.7). There was no significant between-group difference in the risk of adverse events, which were reported in 68.7% of the infants in the vaccine group and in 67.2% of those in the placebo group, or in the risk of serious adverse events (in 8.3% in the vaccine group and in 9.1% in the placebo group); there were 27 deaths in the vaccine group and 22 in the placebo group. None of the infants had confirmed intussusception.

CONCLUSIONS
Three doses of BRV-PV, an oral rotavirus vaccine, had an efficacy of 66.7% against severe rotavirus gastroenteritis among infants in Niger. (Funded by Médecins sans Frontières Operational Center and the Kavli Foundation; ClinicalTrials.gov number, NCT02145000.)

Patent

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Rotavirus Vaccine, Live Attenuated
Oral, Freeze-Dried

US008795686B2

(12) **United States Patent**
Dhere et al.

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

(54) **STABLE, DRIED ROTAVIRUS VACCINE, COMPOSITIONS AND PROCESS FOR PREPARATION THEREOF**

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

(73) 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.

(21) Appl. No.: **13/056,557**

(22) PCT Filed: **Nov. 6, 2009**

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

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Oral, Freeze-Dried

Indian Clinical Trial was a collaborative effort between:

Bill & Melinda Gates Foundation,

PATH

Serum Institute of India Pvt. Ltd.

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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

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Rotavirus Liquid Vaccine

Single Dose Presentation

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Rotavirus Liquid Vaccine

Multi-Mono Dose Presentation

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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.

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Stability

- 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