FOURTEENTH INTERNATIONAL

ROTAVIRUS SYMPOSIUM

MARCH 14–16 **2023** BALI INDONESIA

Learn more on www.sabin.org

Development of Neonatal Rotavirus Vaccine by Bio Farma

14th International Rotavirus Symposium

March 14 – 16 2023, Bali, Indonesia

Adriansjah, PT Bio Farma

Bio Farma in brief

State-owned Enterprise (100 %)
Vaccines & Antisera manufacturer

Established in Aug 6th, 1890 in Jakarta

Relocated to city of Bandung, West Java in 1923

1500 Employees

Implement Integrated System
GMP, GLP, GCP, ISO9001, ISO14001, OHSAS18001, ISO 17025, ISO 27001
ERM, CSR Based ISO 26000

WHO pre-qualified Vac (DTP, DT, TT, DTP-HB, m/b/tOPV, Measles and TT, HB in Uniject, Td, DTP/HB/Hib)

Bio Farma

Base 802899AI (C00429) 11-02

BIO FARMA COVERS 2 SITES

20 KM

The main campus is sited in Pasteur no. 28 Bandung, covering an area of 91 210 sq meters Production, QA and QC activities Marketing and distribution, Finance, Human Capital and Administration.

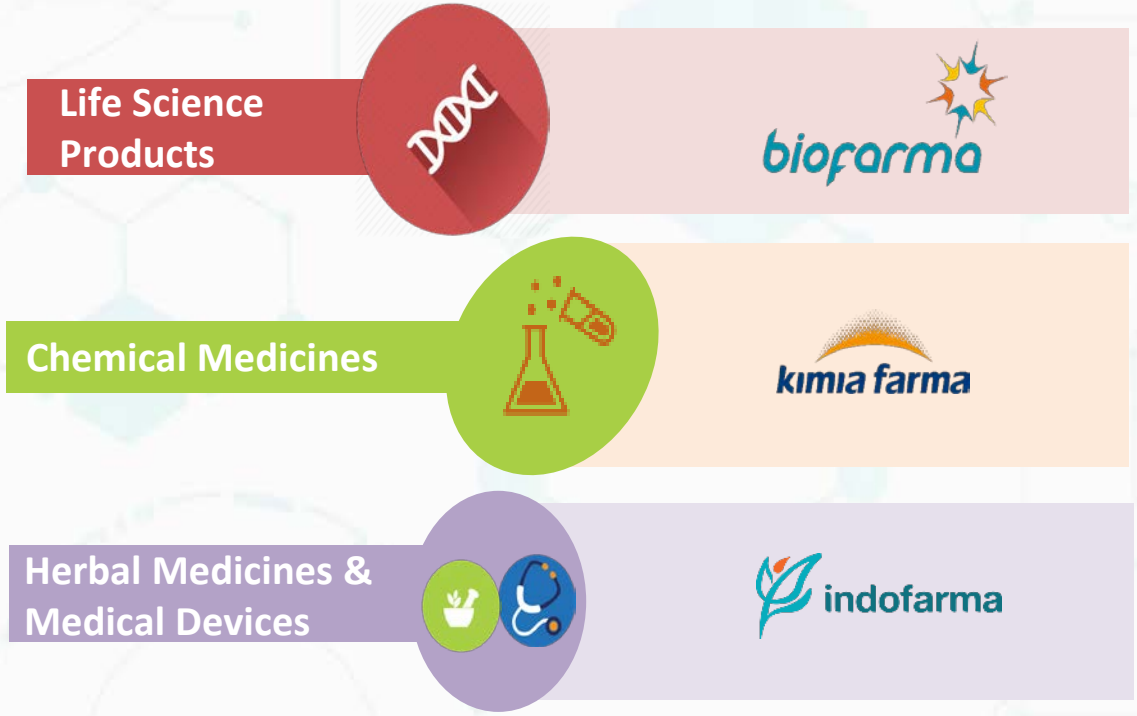
Animal breeding in Cisarua-Lembang (the outskirts of Bandung) covering an area of 282 441 sq meters

Establishment of Indonesia's state-owned Pharmaceutical Holding Company

In early 2020 the Indonesian government established a State-Owned Enterprise (SOE) Healthcare Holding Company by merging three existing SOEs :

- Bio Farma,
- Kimia Farma,
- Indo Farma

Bio Farma has been designated as the parent company.



Key Objectives :

- Provide a comprehensive solution to health and disease problems in Indonesia
- Strengthen self-reliance in Indonesia's national pharmaceutical industry.
- Increase healthcare product availability
- Create joint innovations in the supply of pharmaceuticals and healthcare products to support the future healthcare ecosystem

Bio Farma Vaccines WHO PQ Milestones

Year	Vaccine
1997	OPV, measles 10 ds
2001	DTP, DT, TT (vial)
2003	TT (Uniject)
2004	Hep B (Uniject)
2006	DTP-HepB, measles 20 ds
2009	mOPV1
2010	bOPV 20 ds
2011	Td
2014	DTP/Hb/Hib (Pentabio) 5ds, 10ds
2015	bOPV 10 ds
2019	mOPV2
2020	nOPV2 (WHO EUL)

Others :

- **SEASONAL FLU Vaccine (Flubio), BCG, sIPV,**
- **Antisera : Tetanus, Diphtheria, Snake Venom**

API

1. **Polio bulk**
2. **Measles bulk**
3. **Diphtheria bulk**
4. **Tetanus bulk**
5. **Pertussis bulk**
6. **Hib bulk**

Novel OPV2 (nOPV2) development

World Health Organization | Health Topics | Countries | Newsroom | Emergencies

First ever vaccine listed under WHO emergency use

13 November 2020 | Departmental news | Reading time: 2 min (519 words)

WHO today listed the nOPV2 vaccine (Bio Farma, Indonesia) for emergency use to address the rising cases of a vaccine-derived polio strain in a number of African and East Mediterranean countries. Countries in WHO's Western Pacific and South-East Asia regions are also affected by these outbreaks. The emergency use listing, or EUL, is the first of its kind for a vaccine and paves the way for potential listing of COVID-19 vaccines.

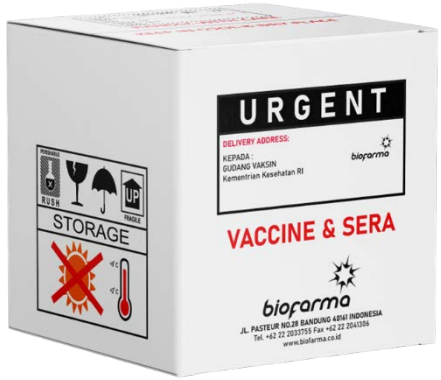
The world has made incredible progress toward polio eradication, reducing polio cases by 99.9% in the last 30 years. But the last steps to ending this disease are proving the most difficult, particularly with continuing outbreaks of circulating vaccine-derived polio viruses (cVDPVs).

- Development in collaboration with Bill & Melinda Gates Foundation (BMGF)
- Development of a type 2 Oral Polio Vaccine that is safer and yet having immunogenicity profile comparable to the current sabin type 2 Oral Polio Vaccine.
- App. 560 mio doses administered across 26 countries since issuance of WHO EUL

Implementation of Global Serialization and Agregation System (Track & Trace)

Primary packaging

Secondary Packaging



Tertiary Packaging

AIDC* Integration

*Automatic Identification & Data Capture

Implemented in Bio Farma's covid vaccine (IndoVac)

BADAN POM

National Agency of Drug and Food Control (NA-DFC)

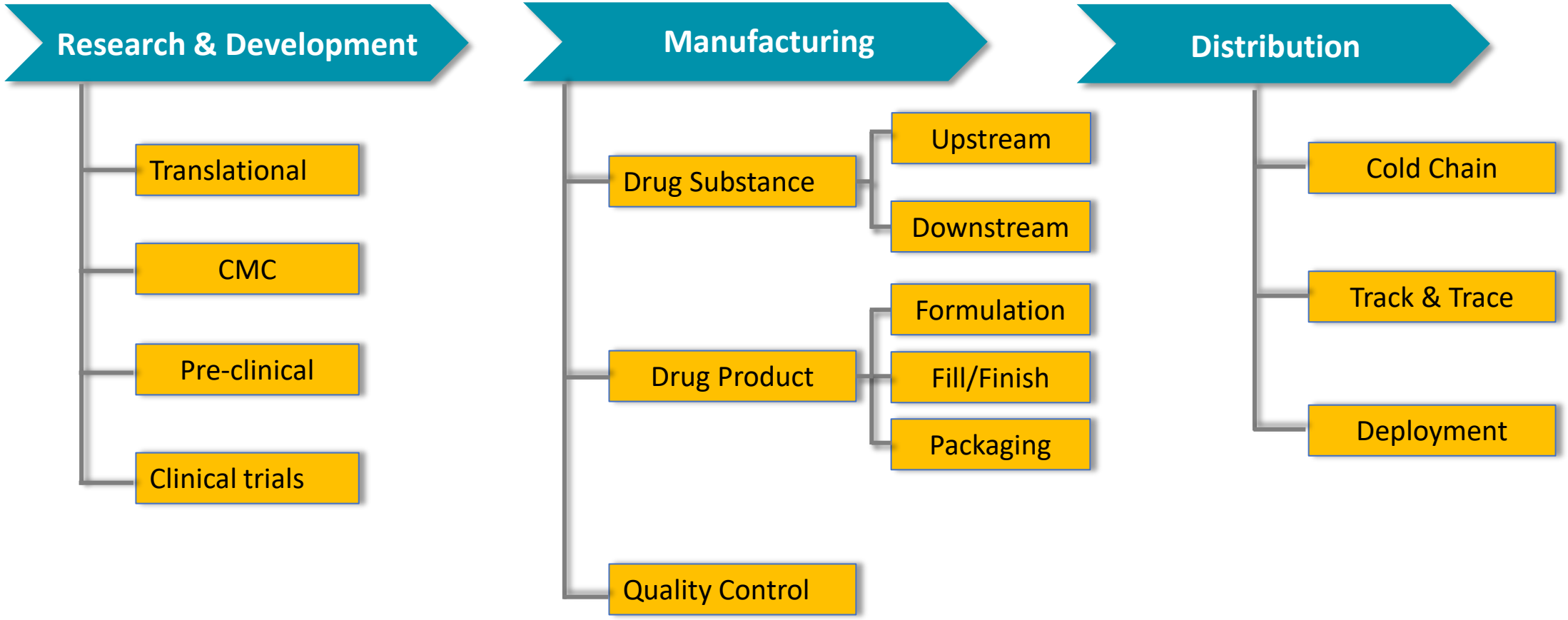
Receiving Product data

Internet

Product data report

TRACK & TRACE
Product information database

Bio Farma's capabilities across the biologics value chain



Bio Farma's Contribution To The World

More Than
152 Countries
Have Used Bio Farma Vaccine Products

More Than
3,2 Billion doses
The production capacity per year

More Than
50 Countries
Member Organisation of Islamic Cooperation

Rotavirus vaccine development

RV3 BB Parent Seed Lot

Transfer technology

University of Gajah Mada, Indonesia (UGM)
Clinical trials

- *Develop a low-cost and commercially viable process for manufacturing* the RV3 rotavirus vaccine
- *Vaccine Formulation* (Alternative formula) for existing formulation

Goal :

To develop and subsequently commercialize attenuated oral rotavirus vaccine in Bio Farma

Considerations in developing rotavirus vaccine

Technology

- Adaptable to current platform : similar to OPV
- Scalable
- Product presentation

Halal

- “non porcine” materials

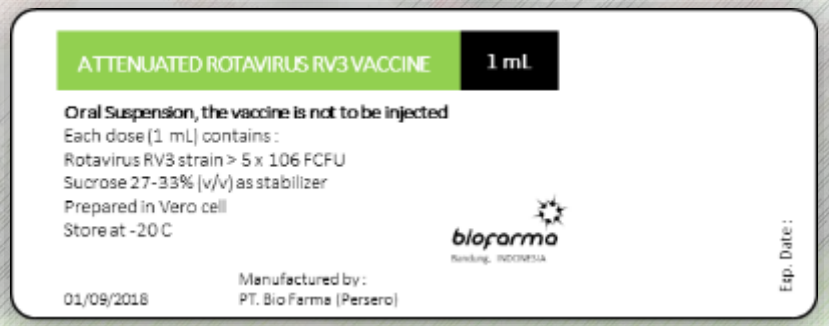
Affordability

- Pricing suitable for national immunization program (public sector)

Development of Rotavirus RV3-BB Vaccine in Bio Farma

RV3-BB Vaccine (liquid Frozen)

- 1mL Frozen-Liquid.
- Stable up to 2 years in -20 C (stability on going)
- Glass vial format, similar to OPV
- Porcine-free !



RV3 ROTAVIRUS VACCINE

RV3 is a ***Naturally Attenuated Human Rotavirus Strain*** (G3P[6]) that was isolated from newborn with asymptomatic diarrhea infection in an obstetric nursery in Melbourne, Australia

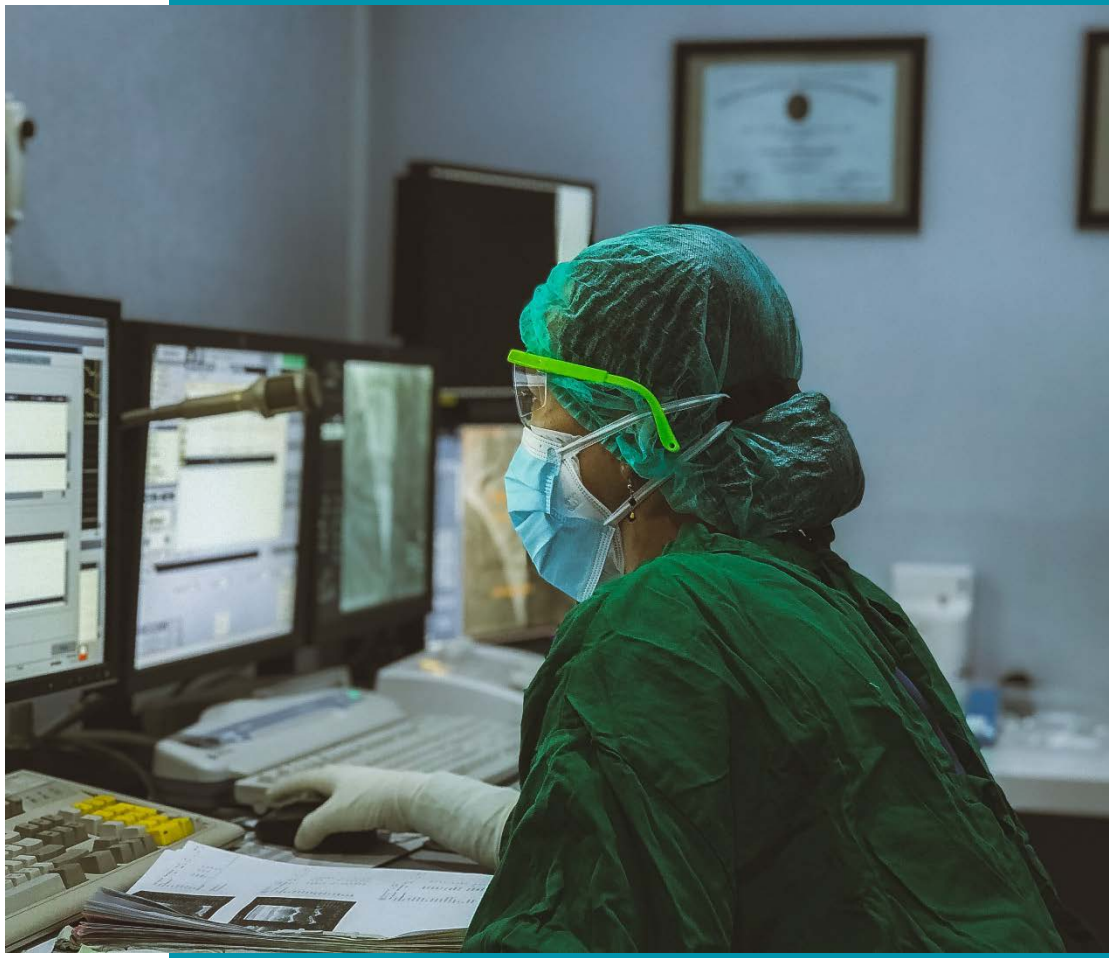
Rotavirus RV3 is suitable for dosing at birth (neonatal vaccine), potentially reducing the incidence of intussusception

Manufactured with non-porcine materials

TARGET PRODUCT PROFILE (TPP)

of Bio Farma Rotavirus Vaccine

Item	Rotavirus - Bio Farma (1 mL)
Compositions	**Rotavirus RV3 Strain**, live attenuated > 5 x 10^6 fcfu/mL Sucrose 30% in DME
Administration route	Oral
Administration dose	3 doses
Co-administered	N/A
Immunization Schedule	**At the age of 0-5 days;** 8-10 weeks; 12-14 weeks
Open Vial policy	Store at +2°C to +8°C for 6 hours; Room temperature for 20 minutes
Storage	≤ - 20° C for 2 years
Presentation	1 dose : 1 ml vial + dropper
Dosage	1 mL
Efficacy	TBA
Trypsin used	**Recombinant**



Clinical trial overview

Phase I

- Randomized, double-blind, placebo-controlled study
- Safety and immunogenicity study in Adults, Children and Neonates
- Results show that the RV3 rotavirus vaccine is well tolerated in all participant cohorts (adults, children, and neonates)
- Publication : https://doi.org/10.1016/j.vaccine.2021.06.071

Phase II

- Randomized double-blind, placebo-controlled trial in Indonesia to evaluate the efficacy of an oral human neonatal rotavirus vaccine (RV3-BB) in preventing rotavirus gastroenteritis
- J.E. Bines, J. At Thobari, C.D. Satria, et.al., Human Neonatal Rotavirus Vaccine (RV3-BB) to Target Rotavirus from Birth. N Engl J Med 2018;378:719-30. DOI:10.1056/NEJMoa1706804. https://www.nejm.org/doi/full/10.1056/nejmoa1706804

Phase III

- Randomized, double-blind, placebo-controlled study
- Efficacy study in neonates
- Final report estimated in September 2023.

Production Plan

- Rota vaccine rolled out in Indonesia estimated in Q4 2024
  - Drug Substance production sharing same facility with another product
  - New facility under construction to meet capacity needs

Thank you!