Food and Drugs Authority (FDA)

Public Assessment Report (PAR)

BIOPOLIO® B1/3 Vaccine

(Bivalent Poliomyelitis Vaccine Type 1&3, Live (Oral)

AVCR005/22 (10 doses) & AVCR006/22 (20 doses)

Bharat Biotech International Ltd. (BBIL), India

PART 1: ABSTRACT

BIOPOLIO® B1/3 (Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral BIOPOLIO® B1/3 contains suspensions of live attenuated poliomyelitis type 1 and 3 viruses (Sabin strains) prepared in Primary Monkey Kidney Cells. BIOPOLIO® B1/3 vaccine is manufactured at Bharat Biotech International Limited, Sy. No. 230, 231 & 235, Genome Valley, Turkapally, Medchal-Malkajgiri District, Telangana – 500078, India.

The Food and Drugs Authority's Guidelines for the registration of human vaccines defines specific evaluation mechanisms for vaccines with stringent standards for quality, safety, and efficacy.

The marketing authorization of BIOPOLIO® B1/3 Vaccine by the FDA is based on reliance pathway in which there was an abridged review of Module 1 to Module 5 of submitted Common Technical Document (CTD) dossier to ascertain the quality, safety, efficacy and sameness of BIOPOLIO® B1/3 vaccine prequalified by WHO.

All accepted presentations of BIOPOLIO® B1/3 have been shown in Part 2 of this report. The approved Patient Information Leaflet (PIL), Summary of Product characteristics (SmPC) and the approved labelling have been presented in Part 3, Part 4 and Part 5 respectively.

Scientific discussion on the quality, nonclinical and clinical aspects of BIOPOLIO® B1/3 have been presented in Part 6 of this report.

The detailed steps taken to approve BIOPOLIO® B1/3 by the FDA have been presented in Part 7 of this report.

No action or steps have been taken following marketing authorization of BIOPOLIO® B1/3.

PART 2: ACCEPTED PRESENTATIONS

FDA Registration Number	Brand Name	Strength	Pharmaceutical Form	Route of Administration	Immediate Packaging	Content (concentration)	Pack size
FDA/HVC/231-07013	BIOPOLIO® B 1/3 10 doses	1*	Aqueous suspension	Oral	Glass vial	1*	Carton of 25 vials (1ml vial of 10 doses & 2ml vial of 20 doses)
FDA/HVC/231-07013	BIOPOLIO® B 1/3 20 doses						

1*= Each dose of 0.1 mL Contains:

- Poliovirus Type 1 (Sabin Strain): NLT 106.0 CCID50
- Poliovirus Type 3 (Sabin Strain): NLT 105.8 CCID50

PART 3: PATIENT INFORMATION LEAFLET (PIL)

Refer to Part 4 for the Summary of Product Characteristics (SmPC) which suffices in the case of vaccines.

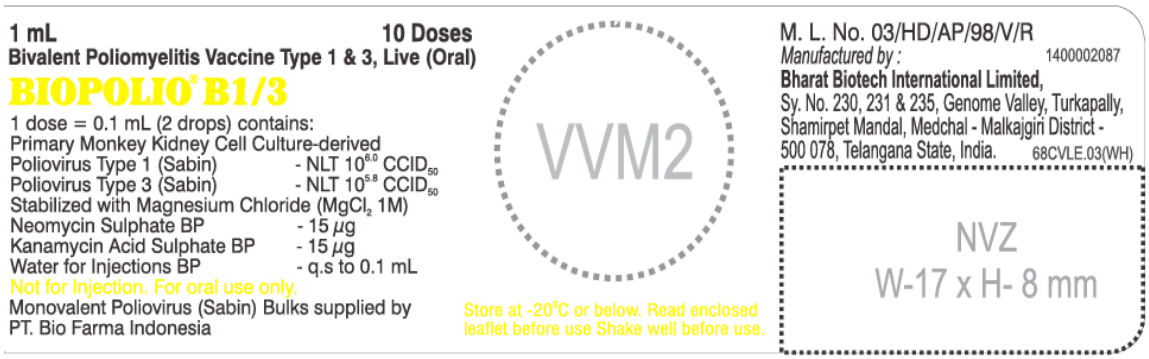
PART 4: SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

Refer to the FDA website below for the SmPC

https://fdaghana.gov.gh/img/smpc/Biopolio%201%20_%203%20SMPCs.pdf

PART 5: LABELLING

1ml Vial (10 doses)



2ml Vial (20 doses)

2 mL **20 Doses**
Bivalent Poliomyelitis Vaccine Type 1 & 3, Live (Oral)
BIOPOLIO® B1/3
1 dose = 0.1 mL (2 drops) contains:
Primary Monkey Kidney Cell Culture-derived
Poliovirus Type 1 (Sabin) - NLT $10^{6.0}$ $CCID_{50}$
Poliovirus Type 3 (Sabin) - NLT $10^{5.8}$ $CCID_{50}$
Stabilized with Magnesium Chloride ($MgCl_2$ 1M)
Neomycin Sulphate BP - 15 µg
Kanamycin Acid Sulphate BP - 15 µg
Water for Injections BP - q.s to 0.1 mL
Not for Injection. For oral use only.
Monovalent Poliovirus (Sabin) Bulks supplied by PT. Bio Farma Indonesia

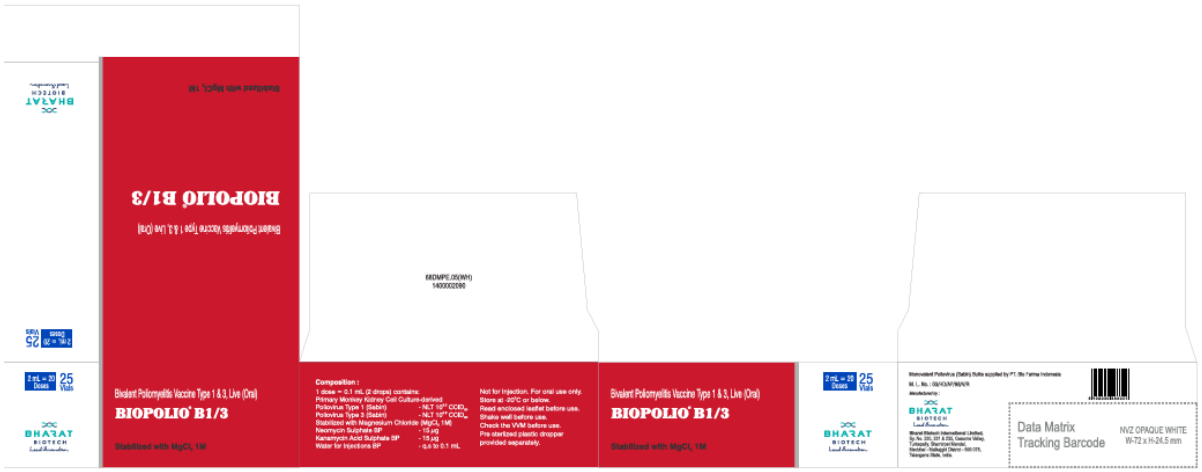
Store at -20°C or below. Read enclosed leaflet before use Shake well before use.

M. L. No. 03/HD/AP/98/V/R
Manufactured by : 1400002089
Bharat Biotech International Limited,
Sy. No. 230, 231 & 235, Genome Valley, Turkapally, Shamirpet Mandal, Medchal - Malkajgiri District - 500 078, Telangana State, India. 68DVLE.04(WH)

NVZ
W-17 x H- 8 mm

1ml (10 doses) Multipack (25 vials) label

2ml (20 doses) Multipack (25 vials) label



PART 6: SCIENTIFIC DISCUSSION

6.0. About the Product: General information:

- **Name of vaccine:** BIOPOLIO® B1/3 (Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live (Oral))
- **Therapeutic indication**: BIOPOLIO® B1/3 is indicated for routine immunization against poliomyelitis in children from birth to 5 years of age, to interrupt transmission of type 1 & type 3 polio viruses.
- **Manufacturer**: Bharat Biotech International Limited, Sy. No. 230, 231 & 235, Genome Valley, Turkapally, Medchal-Malkajgiri District, Telangana – 500078, India
- **Local agent**: Pharmanova Limited, No. 3, Okodan Street, Osu Manhean, Accra-Ghana
- **Pharmaceutical form:** Aqueous Suspension
- **Storage:** The recommended storage temperature for BIOPOLIO® B1/3 is at -20°C or below until the expiry date indicated on the vial. It can be stored up to six months between 2°C and 8°C during its shelf -life. Multi-dose vials of BIOPOLIO® B1/3 from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 28 days after opening, provided that all of the following conditions are met (as described in the WHO Policy Statement: Multi-Dose Vial Policy (MDVP) Revision 2014 WHO/IVB/14.07). Once opened, multi-dose vials should be kept between +2°C and +8°C.
- **Shelf:** 24 months
- **Product presentation:** BIOPOLIO® B 1/3 Drug Product is filled in USP Type 1 moulded glass vials, stoppered with Ready For Use (RFU) grey bromo butyl stoppers and capped with Ready For Use (RFU) tear-down aluminium seals.

6.1 Drug Substance (DS)

6.1.1 Manufacturer

P.T. Bio Farma (Persero) Jalan Pasteur 28, Bandung 40161, Indonesia is the manufacturer of the DS bulk.

6.1.2 Manufacturing Process

The manufacturing of the Bivalent Poliomyelitis Vaccine Type 1 & Type 3, Live, bulk drug substance consists of Cell culturing, virus inoculation, harvest, pooling of harvest, mixing, clarification.

6.1.3 Stability

The stability data shows that the monovalent bulks of poliomyelitis virus Type 1 and Type 3 is stable for 24 months at recommended storage conditions (-70˚± 5˚C) and

supports a shelf life of 24 months from the date of manufacture when stored at the recommended temperature of -20˚ ± 5˚C.

6.2 Drug Product (DP)

6.2.1 DP Manufacturer

Bharat Biotech International Limited, Sy. No. 230, 231 & 235, Genome, Valley, Turkapally, Medchal-Malkajgiri District, Telangana – 500078 India.

6.2.2 Manufacturing Process

The manufacturing process of the finished product involves 3 steps:

I. Formulation
II. Filling, Stoppering and Sealing
III. .Packaging (Inspection, Labelling, Packing and Dispatch)

6.2.3 Stability

Based on the stability data submitted, a shelf life of 24 months has been proposed for the product from the date of manufacture at storage temperature of -20°C ± 5ºC. It can be stored up to six months between 2°C and 8°C during its shelf -life. Multi-dose vials of BIOPOLIO® B1/3 from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 28 days after opening, provided that all of the following conditions are met (as described in the WHO Policy Statement: Multi-Dose Vial Policy (MDVP) Revision 2014 WHO/IVB/14.07). Once opened, multi-dose vials should be kept between +2°C and +8°C.

6.3 Non-clinical Aspects

The monovalent bulks produced by PT Bio Farma have been filled by several manufacturers and have been extensively used in manufacturing of OPV vaccines. OPV vaccines through epidemiological and clinical data, have clearly demonstrated good seroprotection in the target population and well-established literature on its safety. Therefore, no non-clinical studies had been conducted for BIOPOLIO® B 1/3.

6.4 Clinical Aspects

The Marketing Authorization Holder claimed that the clinical studies were performed in accordance with Good Clinical Practice and all applicable regulatory requirements, including, where applicable, the Declaration of Helsinki.

The clinical study below was conducted and submitted by Marketing Authorization Holder for which data submitted for this study is considered satisfactory for clinical safety and efficacy of BIOPOLIO® B 1/3.

- A randomized, multi-centre, double blind, Comparative Phase III study to evaluate the safety and immunogenicity of Bharat Biotech International Limited's monovalent OPV1, Monovalent OPV3 & bivalent OPV 1&3 vaccines (Test vaccines) vs. WHO pre-qualified trivalent OPV (Reference vaccine) healthy neonates.

Part 7: Steps taken for registration

7.1 Submission of the Dossier

The local agent – Pharmanova Limited– representing Bharat Biotech International Limited, Sy. No. 230, 231 & 235, Genome, Valley, Turkapally, Medchal-Malkajgiri District, Telangana – 500078 India, submitted application to the Food and Drugs Authority (FDA) for the registration of BIOPOLIO® B 1/3 10 & 20 doses.

The following are steps taken for the registration of BIOPOLIO® B 1/3.

Receipt of application	• 02nd November 2022
Acknowledgement of Application	• 14th November, 2022
Date of Assessment	• 15th June 2023 – 5th July, 2023
Date of Registration meeting	• 6th July, 2023
Date of Approval	• 2nd August 2023

7.2 Legal basis

The legal basis for the receipt, evaluation, and registration of product is provided below:

- Section 118 (1) of the Public Health Act, 2012, Act 851
- FDA Reliance Policy (FDA/GEN/GDL - 04/01)
- Guidelines for registration of human vaccines (FDA/SMC/BPD/GL-RVC/2014/05)
- SOP for evaluation and registration of a Biological Product application (FDA/VBP/SOP -01).
- SOP for good review practices - Biological Product dossier evaluation (FDA/VBP/SOP -05)

This application was reviewed via the FDA Reliance registration pathway

Part 8: Steps taken following registration.

No action or steps have been taken following marketing authorization of BIOPOLIO® B1/3 vaccine.