SUMMARY OF PRODUCT CHARACTERISTICS

Pentabio Vaccine
(DTP-HB-Hib)

Product Name	**: Pentabio**
Pharmaceutical Form	**: Suspension for injection**
Strength	**: 1, 5 and 10 doses**
Presentation	**: Box of 10 vials @ 0.5 mL**
	Box of 10 vials @ 2.5 mL
	Box of 10 vials @ 5 mL

PT BIO FARMA (PERSERO)
Jl. Pasteur No. 28
Bandung 40161
INDONESIA

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

1.1 Product Name:

Pentabio.

1.2 Strength:

1, 5 and 10 doses.

1.3 Pharmaceutical dosage form:

Suspension for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Pentabio is a homogenous liquid containing purified diphtheria and tetanus toxoids, inactivated whooping cough (pertussis) organism, highly purified, non-infectious particles of hepatitis B surface antigen (HBsAg) and Hib component as bacterial subunit vaccine containing highly purified, non-infectious Haemophilus influenza type b (Hib) capsular polysaccharide chemically conjugated to a protein of tetanus toxoid. The HBsAg is produced by DNA recombinant technology in yeast (*Hansenula polymorpha*) cells. The polysaccharide is derived from Hib bacteria grown in chemically defined media, subsequently purified through a series of ultrafiltration steps. The vaccine is adsorbed onto 3 mg/mL aluminum phosphate. Thimerosal 0.05 mg/mL is used as a preservative. The potency of the vaccine per single human dose is at least 4 IU for pertussis, 30 IU for diphtheria, 60 IU for tetanus (determined in mice), 10 mcg HBsAg and 10 mcg Hib.

Composition:

Each dose (0.5 ml) of vaccine contains:

Purified diphtheria toxoid	20 Lf ($\geq$ 30 IU)
Purified tetanus toxoid	5 Lf ($\geq$ 60 IU)
Inactivated B. pertussis	12 OU ($\geq$ 4 IU)
HBsAg	10 mcg
Hib (PRP-TT)	10 mcg
Al^{3+} as aluminum phosphate	0.33 mg
Thimerosal	0.025 mg

3. PHARMACEUTICAL FORM

Whitish suspension, homogenous after shaking.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

The vaccine is indicated for active primary immunization against diphtheria, tetanus, pertussis, haemophilus influenza type B and hepatitis B diseases.

4.2 Posology and method of administration:

The vaccine should not be used for the birth dose.
In countries where pertussis is of particular danger of young infants, the combination vaccine should be started as soon as possible with the first dose given as early as 6 weeks, and two subsequent doses given at 4-weeks intervals.
The vaccine can be given safely and effectively at the same time as BCG, Measles, Polio (OPV or IPV), Yellow fever vaccine and vitamin A supplementation. If DTP-HB-Hib vaccine is given at the same time as other vaccine, it should be administered at a separate site. It should not be mixed in the vial or syringe with any other vaccine unless it is licensed for use as a combined product.
The liquid vaccine vial should be shaken before use to homogenize the suspension. The vaccine should be injected intramuscularly. The anterolateral aspect of the upper thigh is the preferred site of injection. An injection into a child's buttocks may cause injury to the sciatic nerve and is not recommended. It must not be injected into the skin as this may give rise to local reaction. One dose pediatric is 0.5 mL. A sterile syringe and sterile needle must be used for each injection.

4.3 Contraindications:

Known hypersensitivity to any component of the vaccine or a severe reaction to a previous dose of the combination vaccine or any of its constituents is an absolute contraindication to subsequent doses of the combination vaccine or the specific vaccine know to have provoked an adverse reaction. There are few contraindications to the first dose of DTwP - fits or abnormal cerebral signs in the newborn period or other serious neurogical abnormality are contraindications to the pertussis component. In this case the vaccines should not be given as a combination vaccine but DT should be given instead of DTwP, Hep. B and Hib vaccine given separately. The vaccine will not harm individuals currently or previously infected with the hepatitis B virus.

Immune deficiency
Individuals infected with Human Immunodeficiency Virus (HIV), both asymptomatic and symptomatic, should be immunized with combined vaccine according to standard schedules.

4.4 Special warnings and precautions for use:

- The vaccine should be shaken before use to homogenize the suspension.
- The vaccine should be injected intramuscularly
- An injection into a child's buttocks is not recommended
- A sterile syringe should be used for each injection
- Before use, the information at vaccine vial monitor (VVM) must be followed.

4.5 Interaction with other medicinal products and other forms of interaction:

No interaction studies have been performed.

4.6 Pregnancy and lactation:

No related study has been performed.

4.7 Effects on ability to drive and use machines:

There is no evidence that DTP-HB-Hib Vaccine effects on ability to drive and use machines.

4.8 Undesirable effects:

The type and rate of adverse reactions do not differ significantly from DTP, HB and Hib vaccine reaction given separately.
For DTP, mild local or systemic reactions are common. Some temporary swelling, tenderness and redness at the site of injection together with fever occur in a large proportion of cases. Occasionally severe reaction of high fever, irritability and screaming develop within 24 hours of administration. Hypotonic-hyporesponsive episodes have been reported. Febrile convulsion have been reported at a rate of one per 12500 doses administered. Administration of acetaminophen at time and 4-8 hours after immunization decreases subsequent incidence of febrile reactions. The national childhood encephalophaty study in United Kingdom showed a small increase risk of acute encephalophaty (primarily seizures) following DTP immunization. However, subsequent detail reviews of all available studies by number of groups, including United States Institute of Medicine, The Advisory Committee on Immunization Practices, and The Paediatric Association of Australia, Canada, The United Kingdom and The United States, concluded that the data did not demonstrate a casual relationship between DTwP and chronic nervous system dysfunction in children. Thus there is no scientific evidence that hypotonic-hyporesponsive episode and febrile convulsion have any permanent consequences for the children.
Hepatitis B vaccine is very well tolerated. In placebo-control studies, with the exception of local pain, reported event such a myalgia and transient fever have not been more frequent than in placebo group. Reports of severe anaphylactic reactions are very rare. Available data do not indicate neither casual association between hepatitis B and Guillain-Barré syndrome or demyelinating disorder including multiple sclerosis nor any epidemiological data to support a casual association between hepatitis B vaccination and chronic fatigue syndrome, arthritis, autoimmune disorders, asthma, sudden infant death syndrome or diabetes.
Hib vaccine is very well tolerated. Local reactions may occur within 24 hours of vaccination, where recipients may experience pain and tenderness at the injection site. These reactions are generally mild and transient. In most cases, they spontaneously resolve within two or three days and further medical attention is not required. Mild systemic reactions, including fever, rarely occur following administration of Hib vaccines. More serious reactions are very rare; a causal relationship between more serious reactions and the vaccine has not been established.

4.9 Overdose:

Since registered, we never received report about DTP-HB-Hib Vaccine overdose. No data may support this event.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties:

- Pharmacotherapeutic group : Vaccines
- ATC code : J07CA11
- Mechanism of action (if known) : Stimulates the body to produce antibody against diphtheria, tetanus, pertussis, Hepatitis B, and Hemophilus influenzae B.
- Pharmacodynamic effects : No study has been performed.
- Clinical efficacy and safety : Refer to sections 2.5, 2.7 and module 5 in the Dossier of Adsorbed DTP-HB-Hib Vaccine.

5.2 Pharmacokinetic Properties:

No related study has been performed.

5.3 Preclinical safety data:

No related study has been performed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients:

Al^{3+} as aluminum phosphate
Thimerosal

6.2 Incompatibilities:

No related study has been performed.

6.3 Shelf life:

The shelf life of Pentabio (DTP-HB-Hib) Vaccine is 2 years, stored at +2°C ~ +8°C. The expiry date is shown on the label.

6.4 Special precautions for storage:

Pentabio (DTP-HB-Hib) Vaccine should be stored and transported between +2°C and +8°C, it must not be frozen. Once opened, multi-dose vials should be kept between +2°C and +8°C.

6.5 Nature and contents of container:

Pentabio (DTP-HB-Hib) vaccine are available in 1, 5 and 10 doses in clear vials.
Box of 10 vials @ 0.5 mL (1 dose)
Box of 10 vials @ 2.5 mL (5 doses)
Box of 10 vials @ 5 mL (10 doses)

6.6 Instructions for use, handling and disposal:

- Shake well before use.
- A sterile needle and a sterile syringe should be used for each injection.
- Multi-dose vials of Pentabio (DTP-HB-Hib) from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization session for up to maximum of 4 weeks, provided that all of following condition are met (*as described in the WHO policy statement : The use of opened multi-dose vials in subsequent immunization sessions. WHO/V&B/00.09*):
  - ✓ The expiry date has not passed;
  - ✓ The vaccines are stored under appropriate cold chain conditions;
  - ✓ The vaccine vial septum has not been submerged in water;
  - ✓ Aseptic technique has been used to withdraw all dose;
  - ✓ The vaccine vial monitor (VVM), if attached, has not reached the discard point.

7. MARKETING AUTHORIZATION HOLDER

Biovalys Co., Ltd. Bangkok, Thailand.

8. MARKETING AUTHORIZATION NUMBERS

2C 2/61 (NB)

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization:

Pentabio 1 ds: 17 January 2018

Pentabio 5 ds: 17 January 2018

Pentabio 10 ds: 17 January 2018

Date of renewal of the authorization:

Not applicable.

10. DATE OF REVISION OF THE TEXT

15 May 2018