SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Product Name: Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA) and *Haemophilus influenzae* Type b Conjugate Vaccine (Adsorbed) IP

Brand Name: Easyfive-TT®

Strength: One pediatric dose is 0.5 ml

Pharmaceutical Form: Suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative and quantitative composition for Easyfive-TT® vaccine is as given in table below:-

Single paediatric dose of 0.5 ml contains:

Component	Quantity
Active Ingredients	
Diphtheria Toxoid	20 Lf (30 IU)
Tetanus Toxoid	7.5 Lf (60 IU)
Inactivated w-*B. pertussis*	12 OU (4 IU)
Recombinant Hepatitis B surface antigen (HBsAg)	10 mcg
H. influenzae type b conjugated to Tetanus Toxoid	10 mcg
Inactive Ingredients	
Al^{3+} as Aluminium phosphate gel	0.25 mg
Thiomersal	0.025 mg
Physiological saline	q.s.

* PRP-TT- Purified capsular antigen i.e. Polyribosyl ribitol phosphate (PRP) of *Haemophilus influenzae* type b, conjugated with carrier protein Tetanus Toxoid.

3. PHARMACEUTICAL FORM

The final product has an appearance of a white or almost white material which sediments at the bottom of the container defining two phases: a clear supernatant essentially protein-free composed of physiological saline with the preservative substance dissolved, plus an aluminium phosphate gel with the antigen adsorbed on it. When shaken, a white or almost white suspension is formed, lasting for some minutes, which is the form in which the product is to be administered.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

Easyfive-TT® vaccine is indicated for primary active immunization against Diphtheria, Tetanus, Pertussis, Hepatitis B and severe infections caused by *Haemophilus influenzae* type b in infants from 6 weeks onwards.

4.2 Posology and method of administration:

One paediatric dose is of 0.5 ml.

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, or into the deltoid muscles of older children. 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. 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 known to have provoked an adverse reaction. There are few contraindications to the first dose of DTwP, fits or abnormal cerebral signs or other serious neurological 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 and Hep B and Hib vaccines given separately. The vaccine will not harm individuals currently or previously infected with the Hepatitis B virus.

4.4 Special warnings and precautions for use:

As with other vaccines, the administration of Easyfive-TT® should be postponed in subject suffering from acute severe febrile illness.

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and the possible occurrence of undesirable events) and a clinical examination.

If any of the following events occur in temporal relation to be administration of Easyfive-TT® the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered:

- Temperature of >40.0°C within 48 hours, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hypo-responsive episode) within 48 hours.
- Persistent crying lasting >3 hours, occurring within 48 hours.
- Convulsions with or without fever, occurring within 3 days.

A history of febrile convulsions, a family history of convulsions , a family history of SIDS (Sudden infant Death Syndrome) or a family history an adverse event following Easyfive-TT® vaccination do not constitute contra-indications. Easyfive-TT® should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

As with all injectable vaccine, appropriate medical treatment should always be readily available in case of anaphylactic reactions following the administration of the vaccine. For this reason, the vaccines should remain under medical supervision for 30 minutes after vaccination.

Easyfive-TT® should under no circumstances be administered intravenously or subcutaneously.

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

Easyfive-TT® can be administered simultaneously at separate sites or in any temporal relationship with other paediatric vaccines if the administration is as per the recommended immunization schedule.

As with other intramuscular injections, use with caution in patients on anticoagulant therapy, Immunosuppressive therapies, including irradiations, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses). In patients on these immunosuppressive therapies the immune response to the vaccines may be reduced. Short-term (<2 weeks) corticosteroid therapy or intra-articular, bursal, or tendon injections with corticosteroids would not be immunosuppressive.

Individuals infected with the human immuno-deficiency virus (HIV), both asymptomatic and symptomatic, should be immunized with combined vaccine according to standard schedules.

4.6 Pregnancy and lactation:

Not relevant, as Easyfive-TT® is not intended for use in adult.

4.7 Effects on ability to drive and use machines:

Not relevant, as Easyfive-TT® is not intended for use in adult.

4.8 Undesirable effects:

Side Effects do not differ significantly from the DTwP, HepB and Hib vaccine reactions described separately.

For DTwP, mild local or systemic reactions are common. Some temporary swelling, tenderness and redness at the site of injection together with fever occur in large proportion of cases. Occasionally severe reactions of high fever, irritability and screaming develop within 24 hours of administration. Hypotonic-hyporesponsive episodes have been reported. Febrile convulsions have been reported at a rate of one per 12500 doses administered. Administration of acetaminophen at the time and 4-8 hours after immunization decreases the subsequent incidence of febrile reaction. The national childhood encephalopathy study in United Kingdom showed a small increased risk of acute encephalopathy (primarily seizures) following DTP immunization. However subsequent detailed reviews of all available studies by a number of groups, including the United States Institute of Medicine, the Advisory

Committee on Immunization Practices, and the paediatric associations of Australia, Canada, United Kingdom and United States, concluded that the data did not demonstrate a causal relationship between DTwP and chronic nervous system dysfunction in children. Thus there is no scientific evidence that these reactions have any permanent consequences for children. Hepatitis B vaccine is very well tolerated. In placebo-controlled studies, with the exception of local pain, reported events such as myalgia and transient fever have not been more frequent than in the placebo group. Reports of severe anaphylactic reactions are very rare. Available data do not indicate a causal association between Hepatitis B vaccine and Guillain-Barre syndrome, or demyelinating disorders including multiple sclerosis, nor is there any epidemiological data to support a causal 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. Localized reactions may occur within 24 hours of vaccination, when 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 to three days and further medical attention is not required. Mild systemic reactions, including fever, rarely occur following administration of Hib vaccine. More serious reactions are very rare; a causal relationship between more serious reactions and the vaccine has not been established.

4.9 Overdose:

Not Applicable, as Easyfive-TT® vaccine is administered as per the pediatric immunization schedule under the direct supervision of physicians.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

Diphtheria: Diphtheria is an acute toxin-mediated infectious disease caused by toxigenic strains of *C. diphtheriae*. Protection against disease is due to the development of neutralizing antibodies to the diphtheria toxin; Anti-Diphtheria antibody concentration of 0.1 IU/mL is regarded as protective.

Tetanus: Tetanus is an acute toxin-mediated infectious disease caused by a potent exotoxin released by *C. tetani*. Protection against disease is due to the development of neutralizing antibodies to the tetanus toxin. A serum tetanus antitoxin level of 0.1 IU/mL is considered protective.

Pertussis: Pertussis (whooping cough) is a disease of the respiratory tract caused by *B. pertussis*. The role of the different components produced by *B. pertussis* in either the pathogenesis of, or the immunity to, pertussis is not well understood. There is no well established serological correlate of protection for pertussis.

Hepatitis B: Viral hepatitis caused by hepatitis B virus (HBV) is a major worldwide health problem. Anti HBs concentration of 10mIU/ml is considered protective

Haemophilus influenza type b (Hib): Hib is a leading cause of invasive diseases such as meningitis, bacteraemia, epiglottitis and pneumonia in early childhood. Vaccine engendered antibody directed to the polyribosylribitolphosphate (PRP) capsular polysaccharide has been shown to confer a high level of protection. Anti-PRP antibody concentration of 1 µg / ml is considered protective.

Clinical Studies

Based on study PanBio/CR/0932004/CT, immunogenicity of Pentavalent vaccine was evaluated in 6, 10, 14 weeks schedule (3 doses given at 4 weeks intervals). The immune responses for all the five components of the vaccine was non inferior to the licensed control vaccine. For Anti-diphtheria antibodies- 97.7% of subjects developed protective antibody titers, Anti-tetanus antibodies-99.0% of subjects developed protective antibody titers, Anti-Hib antibodies-89.5% of subjects developed protective antibody titers and Anti-HBs antibodies-97.3% of subjects developed protective antibody titers. For Anti pertussis antibodies, there is no well established Serological correlate of protection. However based on post vaccination anti-PT, Pertussis IgG and post vaccination GMT, the immune response of Pentavalent vaccine was comparable with that of the licensed control vaccine.

5.2 Pharmacokinetic properties:

Not Applicable.

5.3 Preclinical safety data:

Panacea Biotec manufactured the combination vaccines i.e. Easyfive-TT® (DTwP-HepB-Hib) by utilizing the D, T and wP bulk antigens from WHO prequalified supplier P.T. BioFarma, Indonesia and Hepatitis B bulk antigen & Hib (PRP-TT) bulk conjugate from PanEra Biotec Pvt. Ltd., Lalru.

Three individual components i.e. Diphtheria, tetanus and whole cell pertussis imported from M/s. PT. BioFarma, Indonesia are well established one and proven to be safe, as, same are being used successfully since last many decades in immunization history. Further, these components have been prequalified by WHO after successful review of its quality and safety.

Toxicological studies acute, single dose and local tolerance on recombinant Hepatitis B vaccine in swiss mice, guinea pigs and rabbits showed no toxic signs at the tested dose.

HIB-TT conjugate vaccine and Pentavalent vaccine did not produce any adverse effect in Balb/c mice and New Zealand White rabbits with single dose and repeated dose administration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

- Aluminum phosphate gel
- Thiomersal
- Sodium Chloride
- Water for injection

6.2 Incompatibilities:

The vaccine should not be mixed in the vial or syringe with any other vaccines unless it is licensed for use as a combined product.

6.3 Shelf life:

36 months from the date of manufacturing, when stored at 5°C ± 3°C.

Multi-dose vials of Easyfive-TT® 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 provided that all of the following conditions are met (as described in the WHO policy statement: Handling of multi dose vaccine vials after opening, WHO/IVB/14.07):

- The vaccine is currently prequalified by WHO;
- The vaccine is approved for use for up to 28 days after opening the vial, as determined by WHO;

- The vaccine vial has been, and will continue to be, stored at WHO - or manufacturer
- recommended temperatures; furthermore, the vaccine vial monitor, if one is attached, is visible on the vaccine label and is not past its discard point, and the vaccine has not been damaged by freezing.
- The expiry date of the vaccine has not passed;

6.4 Special precautions for storage:

Easyfive-TT® vaccine must be stored and transported at 5°C ± 3°C and can be used until the expiry date indicated on the vial label or the Vaccine Vial Monitor (VVM) changes its color up to the discard point (as mentioned in the patient information leaflet), whichever is earlier.

The vaccine must not be frozen.

6.5 Nature and contents of container:

Nature and contents of container for Easyfive-TT®

Easyfive-TT® vaccine is filled in Single dose (0.5 ml), Two doses (1.0ml), Five doses (2.5ml) and Ten doses (5,0 ml) presentations in USP Type 1 glass vial and stoppered with rubber stopper and sealed with flip off aluminium seal.

Easyfive-TT® vaccine is also filled in single dose Pre-filled syringe of USP type 1 glass containing 0.5 ml vaccine stoppered with plunger stopper.

VVM Type: The labels of Easyfive-TT® vaccine in vial presentations carry VVM 14 (Ref. doc.WHO/V&B/02.35).

7. MARKETING AUTHORIZATION HOLDER:

Panacea Biotec Ltd.
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Tel. : 01795-674036
E-mail : corporate@panaceabiotec.com
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8. MARKETING AUTHORIZATION NUMBER(S)

License No. : MB/07/632

9. DATE OF FIRST AUTHORIZATION/ RENEWAL OF THE AUTHORIZATION

The details of the manufacturing authorization certificates obtained from Licensing Authority, India for Easyfive-TT® vaccine manufactured at Vaccine Formulation Plant (VFP), Baddi, Himachal Pradesh, India are as mentioned below:

- Date of first authorization: March 02, 2009 [in the name of Easyfive with (PRP-TT)]
- Date of authorization with brand name i.e. Easyfive-TT® : August 9, 2012
- Renewal of the authorization: granted on September 29, 2012 valid up to 28.09.2017
- Renewal of the authorization: granted on September 29, 2017 valid up to 28.09.2022.
- Retained up to September 28, 2027