SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

a) Generic Name:

Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA) and Haemophilus Type b Conjugate Vaccine (Adsorbed)

b) Brand Name:

Easyfive®

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One paediatric dose of 0.5 ml contains:

Component	Quantity	Function of component
Active Ingredients		
Diphtheria toxoid	20 Lf (30 IU)	Immunogen
Tetanus Toxoid	7.5 Lf (40 IU in guinea pigs and 60 IU in mice)	Immunogen
Inactivated w-*B.* pertussis	12 OU (4 IU)	Immunogen
rec-Hepatitis B surface antigen (HBsAg)	10 mcg	Immunogen
H. influenzae type b polysaccharide conjugated to Tetanus toxoid (PRP-TT)**	10 mcg	Immunogen
Inactive Ingredients		
Aluminium (Al^{3+}) (As Aluminium Phosphate Gel)	0.25 mg	Adjuvant
Thiomersal	0.025 mg	Antimicrobial Preservative
Physiological saline	q.s.	Diluent

**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

Suspension for Intramuscular Injection.

4. CLINICAL PARTICULARS

4.1 Indications

Easyfive® vaccine (DTwP - Hep B - Hib) is indicated for active immunization against Diphtheria, Tetanus, Pertussis, Hepatitis B and infections caused by *Haemophilus influenzae* type b.

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.

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 in the newborn period 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 HepB 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

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.

DTwP-HepB-Hib vaccine should not be used for the birth dose.

A sterile syringe and sterile needle must be used for each injection.

The expiration date printed on the vial should be checked.

The vaccine must not be frozen.

4.5 Interaction with other medicinal products and other forms of interaction

Easyfive® vaccine can be given safely and effectively at the same time as BCG, measles, polio (OPV or IPV), yellow fever vaccines and vitamin A supplementation. If DTwP-HepB-Hib vaccine is given at the same time as other vaccines, 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.

4.6 Pregnancy and lactation

Not applicable as Easyfive® (DTwP-Hep B-Hib) is not intended for use in adults and adolescents.

4.7 Effects on ability to drive and use machines

Not applicable as Easyfive® (DTwP-Hep B-Hib) is not intended for use in adults and adolescents.

4.8 Undesirable effects

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 a 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 the 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, the United Kingdom and the 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 the 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 it is Single dose vaccine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

In the present pre-licensure study, 660 subjects received 3-dose primary vaccination course of either combined pentavalent Easyfive® vaccine or Tritanrix-HB® reconstituted with Hiberix® (DTwP-HepB/Hib) at 6, 10 and 14 weeks of age. Infants were examined for local reactions at injection sites and for systemic reactions at 30 minutes after each

immunization at the clinic and thereafter on days 1-3 of the dose. Blood samples were collected before administration of the first dose and one month after the third dose for determination of antibody titre levels. 601 subjects completed the study and were evaluated for immunogenicity. For the purpose of statistical analysis, data from all the sites was combined and treated as one data set, and analyzed for immunogenicity and reactogenicity.

With respect to hepatitis anti-HBsAg seroprotection rate (≥ 10 mIU/ml) was 97.3% for Easyfive® and 93.7% for DTwP-HepB/Hib. The upper 95% confidence limit for the treatment difference (DTwP-HepB/Hib – Easyfive®) was -0.2%, which was within the non-inferiority margin of 10%, demonstrating that Easyfive® was non-inferior to DTwP-HepB/Hib. In fact, Easyfive® was superior to DTwP-HepB/Hib, as evidenced by the upper 95% confidence limit for (DTwP-HepB/Hib – Easyfive®) which was less than zero.

The anti-PRP seroprotection rate (≥ 1 µg/ml) was 89.5% for Easyfive® and 94.8% for DTwP-HepB/Hib. The upper 95% confidence limit for the treatment difference (DTwP-HepB/Hib – Easyfive®) was 9.8%, establishing that Easyfive® was non-inferior to DTwP-HepB/Hib.

The anti-diphtheria seroprotection rate (≥ 0.1 IU/ml) was 97.7% for Easyfive® and 94.9% for DTwP-HepB/Hib. The upper 95% confidence limit for the treatment difference (DTwP-HepB/Hib – Easyfive®) was 0.3%, demonstrating that Easyfive® was non-inferior to DTwP-HepB/Hib.

The anti-tetanus seroprotection rate (≥ 0.1 IU/ml) was 99.0% for Easyfive® and 99.3% for DTwP-HepB/Hib, resulting in an upper 95% confidence limit of 1.8% for the treatment difference (DTwP-HepB/Hib – Easyfive®), thus establishing that Easyfive® was non-inferior to DTwP-HepB/Hib.

The pertussis IgG response rate was 30.7% for Easyfive® and 35.2% for DTwP-HepB/Hib. The upper 95% confidence limit of the treatment difference (DTwP-HepB/Hib – Easyfive®) was 12.5%, which was above the non-inferiority margin of 10%. However, the post-vaccination GMTs for the two treatment groups were similar, indicating that Easyfive® was non-inferior to DTwP-HepB/Hib. The wide confidence interval for the treatment difference (DTwP-HepB/Hib – Easyfive®) is attributable to the unusually low response rates (which might be due to calibration problems encountered with the assay that was used). The anti-PT response rate was 35.0% for Easyfive® and 32.1% for DTwP-HepB/Hib vaccine, with an upper 95% confidence limit of 4.8% for the treatment difference (DTwP-HepB/Hib – Easyfive®), demonstrating that Easyfive® was non-inferior to DTwP-HepB/Hib.

Based on the adjusted GMT ratios, it is evident that for Hepatitis B, Diphtheria, and Tetanus, Easyfive® was superior to DTwP-HepB/Hib, since the lower 95% confidence limit of the GMT ratio of Easyfive® over DTwP-HepB/Hib in each case was >1. For pertussis IgG and PT, the GMT ratios of Easyfive® over DTwP-HepB/Hib were approximately 1. In both cases, the lower 95% confidence limit for GMT ratio of Easyfive® over DTwP-HepB/Hib was >0.7, generally considered within the non-inferiority margin. For PRP, the GMT ratio of Easyfive® over DTwP-HepB/Hib was 0.6, with an upper 95% confidence limit >0.7, indicating that Easyfive® was non-inferior to DTwP-HepB/Hib.

5.2 Pharmacokinetic properties

Evaluation of Pharmacokinetic properties is not required for vaccines.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

- Sodium Chloride
- Thiomersal
- Water for injection
- Aluminium Phosphate gel

6.2 Incompatabilities

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

24 months from date of manufacture, when stored at temperature between 5^{o}C±3^{o}C.

6.4 Special precautions for storage

The Easyfive® vaccine must be stored and transported at 5^{o}C±3^{o}C and can be used until the expiry date indicated on the vial label.

The vaccine must not be frozen.

6.5 Nature and contents of the container

0.5 ml of suspension in tubular, colourless glass vial stoppered with bromo butyl rubber closure and finally sealed with flip off aluminium seal.

6.6 Instructions for use and handling

The liquid vaccine vial should be shaken before use to homogenize the suspension.

Each vaccine vial should be carefully inspected for damage or contamination prior to use.

7. Marketing Authorization Holder

a) **Panacea Biotec Ltd.**

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8. Marketing Authorization Number(s)

License No. : MB/07/632

9. Date of first registration/renewal of registration certificate:

Date of first authorisation: March 03, 2009