SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Product Name: Easyfive-TT vaccine [Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA) and *Haemophilus influenzae* Type b Conjugate Vaccine (Adsorbed) (DTwP- Hep B - Hib) – Pentavalent Vaccine]

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	Function of component
Active Ingredients		
Diphtheria Toxoid	20 Lf (30 IU)	Immunogen
Tetanus Toxoid	7.5 Lf (60 IU)	Immunogen
Inactivated w-*B. pertussis*	12 OU (4 IU)	Immunogen
Recombinant Hepatitis B surface antigen (HBsAg)	10 mcg	Immunogen
H. influenzae type b conjugated to Tetanus Toxoid	10 mcg	Immunogen
Inactive Ingredients		
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

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 *Haemophilus influenzae* type b in infants from 6 weeks onwards.

4.2 Posology and method of administration:

Primary vaccination:

One paediatric dose is of 0.5 ml.

Vaccine is given in 3 primary doses at 4-week intervals. 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.

Booster vaccination:

The use of this vaccine for booster dose should be based on National Immunization Program.

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.

The *Easyfive* group and the *DTwP-HepB/Hib* group were similar with regard to the intake of concomitant medications, with 115 (34.7%) subjects in the *Easyfive* group and 110 (33.4%) subjects in the *DTwP-HepB/Hib* group taking at least one concomitant medication. Paracetamol was the most frequent concomitant medication, with 103 (31.1 %) subjects in the *Easyfive* group and 102 (31.0%) subjects in the *DTwP-HepB/Hib*group taking this medication.

Table 1. Number and Percentage of Subjects Who Took At Least One Concomitant Medication, by Type (Total Vaccinated Cohort)

GENERIC NAME	EASYFIVE (N = 331)	DTwP-HEP B/HIB (N = 329)
SUBJECTS TAKING ANY CONCOMITANT MEDICATION	115 (34.7%)	110 (33.4%)
ANTITUSSIVES AND EXPECTORANTS, COMBINATIONS	4 (1.2%)	3 (0.9%)
AZITHROMYCIN	0 (0.0%)	1 (0.3%)
CEPHALEXINE	1 (0.3%)	0 (0.0%)
CEFDINIR	2 (0.6%)	1 (0.3%)
CEFIXIME	1 (0.3%)	0 (0.0%)
COLISTIN	1 (0.3%)	0 (0.0%)
ERYTHROMYCIN	1 (0.3%)	0 (0.0%)
FACTOR IX COMPLEX	0 (0.0%)	1 (0.3%)
LACTOBACILLUS	4 (1.2%)	4 (1.2%)
MEFENAMIC ACID	0 (0.0%)	1 (0.3%)
MULTIVITAMIN	0 (0.0%)	1 (0.3%)
NASAL SALINE	3 (0.9%)	1 (0.3%)
OFLOXACIN	2 (0.6%)	0 (0.0%)
ORAL REHYDRATION SALT	5 (1.5%)	5 (1.5%)
PARACETAMOL	103 (31.1%)	102 (31.0%)
PHOLCODINE	3 (0.9%)	3 (0.9%)
PHYTOMENADIONE	0 (0.0%)	1 (0.3%)
PROMETHAZINE	0 (0.0%)	1 (0.3%)
RACEDOTRIL	0 (0.0%)	1 (0.3%)
SALBUTAMOL	1 (0.3%)	1 (0.3%)

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:

Overall incidence of adverse event.

Based on study PanBio/CR/0932004/CT, the percentages of subjects with any AE (solicited or unsolicited, local or general) reported during the solicited 3-day follow-up period (day 0-3) after each dose, and overall, for each group are presented in Tables 1.

Table 2. Incidence of Any Symptom (Solicited or Unsolicited, Local or General Reported During the 3-Day Follow-up Period after Each Dose (Total Vaccinated Cohort)

	Group	N	n (%)	LL (%)	UL (%)
Dose 1	EASYFIVE	331	219 (66.2 %)	60.8	71.2
	DTwP-HEP B/HIB	329	217 (66.0 %)	60.6	71.1
Dose 2	EASYFIVE	322	195 (60.6 %)	55.0	65.9
	DTwP-HEP B/HIB	320	203 (63.4 %)	57.9	68.7
Dose 3	EASYFIVE	312	170 (54.5 %)	48.8	60.1
	DTwP-HEP B/HIB	315	151 (47.9 %)	42.3	53.6
Overall/Subject	EASYFIVE	331	259 (78.2 %)	73.4	82.6
	DTwP-HEP B/HIB	329	261 (79.3 %)	74.5	83.6

SOLICITED LOCAL ADVERSE EVENTS

The overall incidence of any local symptom reported during the 3-day follow-up period after vaccination, was similar for the two groups. In both groups, the incidence of any local symptom decreased from Dose 1 to Dose 2 and from Dose 2 to Dose 3.

Table 3. Incidences of Local Symptoms Reported During the 3-Day Follow-up Period after Each Dose (Total Vaccinated Cohort)

		EASYFIVE					DTwP-HEP B/HIB					Fisher's p value
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	
DOSE 1												
Area of redness	ALL	331	78	23.6	19.1	28.5	329	79	24.0	19.5	29	0.0206
	Mild		78	23.6	19.1	28.5		71	21.6	17.3	26.4	
	Moderate		0	0.0	0	1.1		7	2.1	0.9	4.3	
	Severe		0	0.0	0	1.1		1	0.3	0	1.7	
Hardness	ALL	331	54	16.3	12.5	20.7	329	67	20.4	16.1	25.1	0.0483
	Mild		50	15.1	11.4	19.4		52	15.8	12	20.2	
	Moderate		4	1.2	0.3	3.1		14	4.3	2.3	7	
	Severe		0	0.0	0	1.1		1	0.3	0	1.7	
Swelling	ALL	331	94	28.4	23.6	33.6	329	86	26.1	21.5	31.2	0.6641
	Mild		78	23.6	19.1	28.5		73	22.2	17.8	27.1	
	Moderate		16	4.8	2.8	7.7		12	3.6	1.9	6.3	
	Severe		0	0.0	0	1.1		1	0.3	0	1.7	
Tenderness	ALL	331	79	23.9	19.4	28.8	329	76	23.1	18.7	28	0.7131
	None		65	19.6	15.5	24.3		60	18.2	14.2	22.8	
	Interfered with movement of leg		14	4.2	2.3	7		16	4.9	2.8	7.8	
DOSE 2												
Area of redness	ALL	322	58	18.0	14	22.7	320	60	18.8	14.6	23.5	0.9484
	Mild		55	17.1	13.1	21.6		57	17.8	13.8	22.5	
	Moderate		3	0.9	0.2	2.7		3	0.9	0.2	2.7	
	Severe		0	0.0	0.0	0.0		0	0.0	0.0	0.0	
Hardness	ALL	322	52	16.1	12.3	20.6	320	50	15.6	11.8	20.1	0.5335
	Mild		49	15.2	11.5	19.6		44	13.8	10.2	18	
	Moderate		3	0.9	0.2	2.7		6	1.9	0.7	4	
	Severe		0	0.0	0.0	0.0		0	0.0	0.0	0.0	
Swelling	ALL	322	80	24.8	20.2	29.9	320	79	24.7	20.1	29.8	
	Mild		76	23.6	19.1	28.6		65	20.3	16	25.1	

		EASYFIVE					DTwP-HEP B/HIB					Fisher's p value
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	
	Moderate		4	1.2	0.3	3.1		14	4.4	2.4	7.2	0.0369
	Severe		0	0.0	0.0	0.0		0	0.0	0.0	0.0	
Tenderness	ALL	322	76	23.6	19.1	28.6	320	65	20.3	16	25.1	1.000
	None		61	18.9	14.8	23.7		51	15.9	12.1	20.4	
	Interfered with movement of leg		15	4.7	2.6	7.6		14	4.4	2.4	7.2	
DOSE 3												
Area of redness	ALL	312	45	14.4	10.7	18.8	315	37	11.7	8.4	15.8	0.3446
	Mild		45	14.4	10.7	18.8		37	11.7	8.4	15.8	
	Moderate		0	0.0	0.0	0.0		0	0.0	0.0	0.0	
	Severe		0	0.0	0.0	0.0		0	0.0	0.0	0.0	
Hardness	ALL	312	43	13.8	10.2	18.1	315	31	9.8	6.8	13.7	0.2257
	Mild		42	13.5	9.9	17.8		30	9.5	6.5	13.3	
	Moderate		1	0.3	0	1.8		1	0.3	0	1.8	
	Severe		0	0.0	0.0	0.0		0	0.0	0.0	0.0	
Swelling	ALL	312	51	16.3	12.4	20.9	315	46	14.6	10.9	19	0.4383
	Mild		47	15.1	11.3	19.5		45	14.3	10.6	18.6	
	Moderate		4	1.3	0.4	3.2		1	0.3	0	1.8	
	Severe		0	0.0	0.0	0.0		0	0.0	0.0	0.0	
Tenderness	ALL	312	55	17.6	13.6	22.3	315	49	15.6	11.7	20	0.2778
	None		47	15.1	11.3	19.5		35	11.1	7.9	15.1	
	Interfered with movement of leg		8	2.6	1.1	5		14	4.4	2.5	7.3	
Overall/Subject												
Area of redness	ALL	331	96	29.0	24.2	34.2	329	102	31.0	26	36.3	0.1523
	Mild		93	28.1	23.3	33.3		91	27.7	22.9	32.8	
	Moderate		3	0.9	0.2	2.6		10	3.0	1.5	5.5	
	Severe		0	0.0	0	1.1		1	0.3	0	1.7	
Hardness	ALL	331	81	24.5	19.9	29.5	329	91	27.7	22.9	32.8	0.0920
	Mild		73	22.1	17.7	26.9		71	21.6	17.3	26.4	
	Moderate		8	2.4	1	4.7		19	5.8	3.5	8.9	
	Severe		0	0.0	0	1.1		1	0.3	0	1.7	
Swelling	ALL	331	140	42.3	36.9	47.8	329	136	41.3	36	46.9	0.9528
	Mild		117	35.3	30.2	40.8		112	34.0	28.9	39.4	
	Moderate		23	6.9	4.5	10.2		23	7.0	4.5	10.3	
	Severe		0	0.0	0	1.1		1	0.3	0	1.7	
Tenderness	ALL	331	107	32.3	27.3	37.7	329	98	29.8	24.9	35	0.3633
	None		87	26.3	21.6	31.4		72	21.9	17.5	26.7	
	Interfered with movement of leg		20	6.0	3.7	9.2		26	7.9	5.2	11.4	

The incidence of each local symptom over all doses was similar for the groups, except at dose 1 when the incidences of area of redness and hardness were significantly (p = 0.0206 and 0.0483, respectively) higher for the *DTwP-HepB/Hib* group, compared to the *Easyfive* group, and at dose 2 when the incidence of swelling was significantly (p = 0.0369) higher for the *Easyfive* group, compared to the *DTwP-HepB/Hib* group. The most frequent local symptom was swelling (42.3% overall in the *Easyfive* group and 41.3% overall in the *DTwP-HepB/Hib* group).

SOLICITED GENERAL ADVERSE EVENTS

The overall incidence of any general symptom reported during the 3-day follow-up period after vaccination, was similar for the two groups. In both groups, the incidence of any general symptom decreased from Dose 1 to Dose 2 and from Dose 2 to Dose 3.

Table 4 Incidences of General Symptoms Reported during the 3-day Follow-up Period after Each Dose (Total Vaccinated Cohort)

		EASYFIVE					DTwP-HEP B/HIB					Fisher's P-Value
					95% CI					95% CI		
Dose	Symptoms	N	n	%	LL	UL	N	n	%	LL	UL	
DOSE 1	Lot fussier/crying	331	32	9.7	6.7	13.4	329	30	9.1	6.2	12.8	0.8940
	Restless	331	17	5.1	3	8.1	329	15	4.6	2.6	7.4	0.8566
	Sleepier	331	13	3.9	2.1	6.6	329	12	3.6	1.9	6.3	1.0000
	Eating poorly	331	14	4.2	2.3	7	329	11	3.3	1.7	5.9	0.6843
	Vomiting	331	9	2.7	1.3	5.1	329	10	3.0	1.5	5.5	0.8208
	Diarrhoea	331	6	1.8	0.7	3.9	329	10	3.0	1.5	5.5	0.3252
	Warm to touch	331	195	58.9	53.4	64.3	329	182	55.3	49.8	60.8	0.3870
DOSE 2	Lot fussier/crying	322	24	7.5	4.8	10.9	319	34	10.7	7.5	14.6	0.1709
	Restless	322	12	3.7	1.9	6.4	319	12	3.8	2	6.5	1.0000
	Sleepier	322	8	2.5	1.1	4.8	319	8	2.5	1.1	4.9	1.0000
	Eating poorly	322	8	2.5	1.1	4.8	319	14	4.4	2.4	7.3	0.2011
	Vomiting	322	13	4.0	2.2	6.8	319	7	2.2	0.9	4.5	0.2556
	Diarrhoea	322	9	2.8	1.3	5.2	319	11	3.4	1.7	6.1	0.6578
	Warm to touch	322	175	54.3	48.7	59.9	319	176	55.2	49.5	60.7	0.8744
DOSE 3	Lot fussier/crying	312	24	7.7	5	11.2	315	32	10.2	7.1	14	0.3274
	Restless	312	9	2.9	1.3	5.4	315	9	2.9	1.3	5.4	1.0000
	Sleepier	312	8	2.6	1.1	5	315	8	2.5	1.1	4.9	1.0000
	Eating poorly	312	5	1.6	0.5	3.7	315	8	2.5	1.1	4.9	0.5770
	Vomiting	312	7	2.2	0.9	4.6	315	4	1.3	0.3	3.2	0.3815
	Diarrhoea	312	7	2.2	0.9	4.6	315	10	3.2	1.5	5.8	0.6243
	Warm to touch	312	142	45.5	39.9	51.2	315	124	39.4	33.9	45	0.1253
Overall / Subject												
	Lot fussier/crying	331	44	13.3	9.8	17.4	329	54	16.4	12.6	20.9	0.2750
	Restless	331	23	6.9	4.5	10.2	329	26	7.9	5.2	11.4	0.6589
	Sleepier	331	18	5.4	3.3	8.5	329	20	6.1	3.8	9.2	0.7414
	Eating poorly	331	17	5.1	3	8.1	329	23	7.0	4.5	10.3	0.3327
	Vomiting	331	18	5.4	3.3	8.5	329	18	5.5	3.3	8.5	1.0000
	Diarrhoea	331	14	4.2	2.3	7	329	24	7.3	4.7	10.7	0.0972
	Warm to touch	331	246	74.3	69.3	78.9	329	243	73.9	68.8	78.5	0.9293

The incidence of each solicited general symptom at each dose and over all doses was similar for the two groups, with no statistically significant differences. The most frequent solicited general symptom was 'warm to touch' (74.3% overall in the *Easyfive* group and 73.9% overall in the *DTwP-HepB/Hib* group).

UNSOLICITED ADVERSE EVENTS

Table 8.10 presents the percentage of subjects with unsolicited signs or symptoms (regardless of relationship to vaccination) reported within 30 days after vaccination. It includes all subjects with AEs that were not included in the summaries of local or general symptoms occurring within the 3-day follow-up period after vaccination.

Table 5. Percentage of Subjects with Unsolicited Symptoms Classified by medDRA System Organ Class and Preferred Term within 30 Dyas after Vaccination (Total Vaccinated Cohort)

SYSTEM ORGAN CLASS	PREFERRED TERM	EASYFIVE (N=331)	DTwP-HEP B/HIB (N=329)
ALL SYSTEMS	ANY ADVERSE EVENT	3 (0.9%)	4 (1.2%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	ANY ADVERSE EVENT	2 (0.6%)	2 (0.6%)
	INJECTION SITE SWELLING	2 (0.6%)	1 (0.3%)
	PYREXIA	0 (0.0%)	1 (0.3%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	ANY ADVERSE EVENT	0 (0.0%)	2 (0.6%)
	COUGH	0 (0.0%)	1 (0.3%)
	DYSPNOEA	0 (0.0%)	1 (0.3%)
	NASOPHARYNGITIS	0 (0.0%)	1 (0.3%)
CONGENITAL FAMILIAL GENETIC DISORDERS	ANY ADVERSE EVENT	1 (0.3%)	0 (0.0%)
	MICROCEPHALY	1 (0.3%)	0 (0.0%)
HEPATOBILIARY DISORDERS	ANY ADVERSE EVENT	0 (0.0%)	1 (0.3%)
	JAUNDICE	0 (0.0%)	1 (0.3%)

The incidence of unsolicited AEs was similar (3 (0.9%) for *Easyfive* group and 4 (1.2%) for *DTwP-HepB/Hib* group) for the two groups. The most frequently reported unsolicited symptom was injection site swelling (2 (0.6%) in the *Easyfive* group and 1 (0.3%) in the *DTwP-HepB/Hib* group), which, in all 3 cases, was possibly related to the study vaccine.

SERIOUS ADVERSE EVENTS

Fatal Events

There were no deaths.

Non-fatal Events

Non-fatal SAEs were reported for 5 subjects (1 (0.3%) subject in the *Easyfive* group and 4 (1.2%) subjects in the *DTwP-HepB/Hib),* as shown in Table 8.12, all with doubtful relationship to the study vaccine. The subjects were not withdrawn from the study, and they recovered completely.

Table 6. Subjects with Serious Adverse Events Reported During the Study (Total Vaccinated Cohort)

TREATMENT	SUBJECT NO	START DATE	END DATE	NATURE OF SAE	CAUSALITY	OUTCOME
EASYFIVE	E5113	13/04/07	-	MICROCEPHALY	Doubtful	Complete Recovery
DTwP-HEP B/HIB	E2055	06/12/06	06/12/06	BLEEDING AT SITE OF INJECTION	Doubtful	Complete Recovery
DTwP-HEP B/HIB	E5007	24/09/06	30/09/06	COUGH, COLD, FEVER AND BREATHLESSNESS	Doubtful	Complete Recovery
DTwP-HEP B/HIB	E5045	17/10/06	21/10/06	COUGH, FEVER AND BREATHLESSNESS	Doubtful	Complete Recovery
DTwP-HEP B/HIB	E6062	01/11/06	16/12/06	JAUNDICE	Doubtful	Complete Recovery

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. Based on the information sheet observed rate of vaccine reactions of Diphtheria, Pertussis, Tetanus vaccines, 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.

Based on the study related to Hepatitis B Vaccines in the article of Journal Infectious Diseases, 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.

In a randomize clinical study of Easyfive vaccine in healthy infants following adverse events was reported. Very common ≥ 1/10, Common ≥ 1/100 to < 1/10, Uncommon ≥ 1/1000 to < 1/100, Rare ≥ 1/10000 to < 1/1000, Very Rare < 1/10000.

System Organ Class	Frequency	Adverse Events
General disorders and administration site conditions	Very common	Pain/tenderness, Fever, Swelling, Redness, warm to touch
Psychiatric disorders	Common	Lot fussier/Crying, Restless
Gastrointestinal disorders	Common	Vomiting, Diarrhea
Nervous system disorders	Common	Sleepier
Metabolism and nutrition disorder	Common	Poor eating
Congenital Familial Genetic disorder	Rare	Microcephaly

4.9 Overdose:

No case of overdose has been reported.

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.

28 days after opening of the vial, when stored at recommended storage temperature of 2-8°C.

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, Single dose vial

Box, 25 vial @ 10 doses (5 mL)

The vaccine in Single Pediatric dose (0.5 ml) is filled in USP Type 1 glass vial (2.0 ml) with 13 mm grey bromo butyl rubber stopper and sealed with 13 mm flip off aluminium seal.

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

7. MARKETING AUTHORIZATION HOLDER

Imported and distributed by:

PT Bio Farma (Persero)

Jl. Pasteur No. 28

Bandung, Indonesia

Tel. : +62 22 2033755

Fax : +62 22 2041306

E-mail : mail@biofarma.co.id

Produced by:

Panacea Biotec Ltd.

Malpur, Baddi, Distt Solan,

Himachal Pradesh – 173205, India

Tel. : +91- 1795-304000

Fax : +91-1795-304005

E-mail : corporate@panaceabiotec.com

8. MARKETING AUTHORIZATION NUMBER(S)

License No. :

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

HARUS DENGAN RESEP DOKTER

INFORMASI PRODUK UNTUK PASIEN

Vaksin Easyfive® **SUSPENSI INJEKSI**
Vaksin Kombinasi Difteri, Tetanus, Pertusis (DTP), Hepatitis-B Rekombinan (HB) dan Haemophilus influenza tipe b (Hib)
(Kombinasi dan Jerap)

Informasi Produk (PIL) ini mengandung informasi yang dapat membantu untuk mengetahui manfaat dan risiko penggunaan **Vaksin Easyfive®** yang sudah atau akan Anda terima. Bicarakan kepada Tenaga Kesehatan yang merawat Anda apabila ada pertanyaan lebih lanjut.

Apa itu Vaksin Easyfive®?
"**Vaksin Easyfive®**" merupakan vaksin yang mengandung toksoid difteri dan tetanus murni, bakteri pertusis (penyebab batuk rejan) yang tidak aktif, antigen permukaan rekombinan Hepatitis B (HBsAg), polisakarida *Haemophilus influenzae* tipe b yang terkonjugasi dengan toksoid tetanus dan bahan inaktif lainnya.

Apa yang terkandung dalam Vaksin Easyfive®?
Dalam setiap 0,5 mL **Vaksin Easyfive®** mengandung Toksoid Diphteria 20 Lf (30 IU); Toksoid Tetanus 7.5 Lf; *B. pertussis* (sel utuh) 12 OU (4 IU), HBsAg (rDNA) 10 mcg; Polisakarida kapsul yang dimurnikan terkonjugasi dengan Toksoid Tetanus (protein pembawa) 10 mcg; aluminium fosfat Al^{+++} 0.25 mg; dan pengawet Thiomersal 0.25 mg.

Untuk apa Vaksin Easyfive® digunakan?
Vaksin Easyfive® digunakan sebagai imunisasi aktif terhadap Difteri, Tetanus, Pertusis, Hepatitis B dan infeksi yang disebabkan oleh *Haemophilus influenzae* tipe b pada bayi 6 bulan ke atas.

Bagaimana jadwal vaksinasi untuk Vaksin Easyfive®?
Dosis imunisasi **Vaksin Easyfive®**dianjurkan untuk diberikan sebanyak tiga dosis masing-masing 0,5 ml dengan jarak antar dosis empat minggu dimulai pada usia 6 minggu.

Siapa yang tidak boleh divaksinasi dengan Vaksin Easyfive®?
Vaksin Easyfive® tidak diperbolehkan diberikan pada setiap orang yang:
- Bayi baru lahir
- Alergi/hipersensitif terhadap setiap komponen vaksin,
- Hamil dan menyusui,
- Mengalami reaksi anafilaksis (reaksi alergi berat) yang berhubungan dengan vaksin pada dosis sebelumnya.
- Adanya tanda-tanda gangguan serebral pada masa bayi baru lahir atau kelainan neurologis serius lainnya merupakan kontraindikasi terhadap komponen pertusis.

Bagaimana saya mendapatkan Easyfive®?
Vaksin Easyfive® tersedia dalam bentuk suspensi injeksi berwarna keputihan dan homogen setelah dikocok.
Vaksin Easyfive® akan disuntikan ke dalam otot (intramuscular) sebanyak 0.5 mL. Bagian tubuh paha atas adalah tempat penyuntikan yang paling direkomendasikan atau ke dalam

otot lengan atas pada anak yang secara usia lebih besar. Suntikan di bokong anak tidak dianjurkan karena dapat menyebabkan cedera pada saraf. Tidak boleh disuntikan ke dalam kulit karena akan menyebabkan reaksi lokal.
Untuk imunisasi booster diberikan mengikuti Program Imunisasi Nasional.

Apa yang perlu diperhatikan saat menggunakan Vaksin Easyfive®?
Terdapat beberapa hal yang perlu diperhatikan ketika menggunakan **Vaksin Easyfive®**, yaitu:

- Laporkan ke petugas kesehatan informasi mengenai riwayat reaksi sebelumnya terhadap vaksin atau vaksin serupa, riwayat vaksinasi sebelumnya, status kesehatan saat ini.
- Tanyakan pada petugas kesehatan mengenai manfaat dan risiko vaksinasi., dan juga menanyakan status kesehatan anak.
- Terdapat peningkatan risiko kejang setelah pemberian vaksin yang mengandung DTP pada anak yang mempunyai riwayat kejang dalam keluarga dan harus segera mendapat perawatan medis yang tepat jika terjadi kejang.
- Penerima vaksin perlu diobservasi selama 30 menit pasca vaksinasi.
- Laporkan ke tenaga kesehatan terkait kejadian yang berkaitan dengan vaksinasi.

Obat dan Makanan apa yang harus dihindari jika menggunakan Vaksin Easyfive®?
Vaksin Easyfive® tidak boleh dicampur dengan vaksin lain dalam satu syringe. Belum terdapat informasi terkait makanan atau obat yang harus dihindari ketika menggunakan **Vaksin Easyfive®**

Apakah Vaksin Easyfive® boleh digunakan pada wanita hamil dan menyusui?
Vaksin Easyfive® ini tidak boleh diberikan pada wanita hamil dan menyusui.

Dapatkah Vaksin Easyfive® diberikan bersamaan dengan vaksin lain?
Vaksin Easyfive® dapat diberikan secara aman dan efektif bersamaan dengan vaksin BCG, campak, polio (OPV atau IPV), vaksin *yellow fever*, dan pemberian vitamin A. Jika **Vaksin Easyfive®** diberikan bersamaan dengan vaksin lainnya, maka vaksin tersebut harus diberikan di lokasi yang terpisah. Pemberian vaksin pada waktu yang bersamaan dapat dilakukan dengan cara penyuntikan dilakukan di lokasi suntikan yang berbeda serta menggunakan alat suntik yang berbeda.

Dapatkah saya mengemudi atau mengoperasikan mesin setelah vaksinasi dengan Vaksin Easyfive®?
Vaksin Easyfive® ini tidak diperuntukan untuk orang dewasa

Apa efek samping yang mungkin terjadi setelah pemberian Vaksin Easyfive®?
Efek samping yang mungkin terjadi meliputi pembengkakan yang sifatnya sementara, nyeri tekan dan kemerahan di tempat suntikan disertai demam, iritabilitas, menangis terus menerus, atau nyeri otot serta demam sampai demam tinggi. Tidak ada kejadian overdosis yang pernah dilaporkan.

Bagaimana cara penyimpanan Vaksin Easyfive®?
Vaksin Easyfive® dapat disimpan 24 bulan sejak tanggal produksi, bila disimpan pada suhu antara 5°C±3°C. **Vaksin Easyfive®** harus disimpan dan dipindahkan pada suhu 5°C ± 3°C serta dapat digunakan sampai tanggal kadaluarsa yang tertera pada label vial.
Vaksin Easyfive® dapat digunakan hingga 28 hari setelah vial dibuka dan harus disimpan pada suhu penyimpanan yang direkomendasikan antara 2 - 8°C.

No. reg:

Diproduksi oleh:
Panacea Biotec Ltd. Malpur, Baddi, Distt Solan,
Himachal Pradesh – 173205, India

Didaftarkan oleh:
PT Bio Farma (Persero)
Jl. Pasteur No.28
Bandung, Indonesia

“HARUS DENGAN RESEP DOKTER”

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