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Experience with the first wP based fully liquid hexavalent vaccine.

EasySix™ Vaccine

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EasySix

FULLY LIQUID wP BASED HEXAVALENT COMBINATION VACCINE

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- What is EasySix ?
- Clinical development plan
- Safety profile
- Immunogenicity
- Conclusions

WHAT IS EasySix® : Composition and Présentation

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Fully Liquid Hexavalent Vaccine, each dose of 0.5 ml contains:

Ingredients	Quantity per dose of 0.5 ml
Active Component	**Unit /Dose**
Diphtheria toxoid	≥ 30 IU
Tetanus toxoid	≥ 60 IU
Inactivated w-*Bordetella pertussis*	≥ 4 IU
r Hepatitis B surface antigen	≥ 10 µg
Haemophilus influenzae type b conjugated (PRP-TT)	10 µg
Inactivated Salk Polio Virus type 1 Inactivated Salk Polio Virus type 2 Inactivated Salk Polio Virus type 3	40 DU 8 DU 32 DU
Inactive Component	
Al^{3+} as Aluminium phosphate gel	NMT 1.25 mg
2-phenoxyethanol	3.3 mg
Physiological saline	q.s to 0.5 ml

EasySix®: Clinical Development Plan

Clinical Studies

Phase I Study	Phase II Study
Safety in toddlers : India EasySix® : n = 24 15-18 months	Efficacy & Safety in infants - India EasySix® : n = 136 VS PENTAVAC™ + IMOVAX® : n = 136 6 - 10 weeks

Goals of Clinical Development

- To assess the safety and tolerability of fully liquid hexavalent DTwP-HepB-Hib-IPV vaccine (EasySix□)
- To show that the hexavalent combination vaccine is safe and induces protective immune responses equivalent (non-inferior) to previously licensed combination vaccines PENTAVAC™ and IMOVAX®
- To support the use of the vaccine with vaccination regimen : 6, 10 and 14 weeks

Clinical Study

Study Title: To assess the safety and tolerability of fully liquid hexavalent DTwP-Hep B-Hib-IPV vaccine (EasySix®) of Panacea Biotec Ltd. in healthy subjects

Sr. No.	Parameters	Results
1	**No. of Healthy Subjects (Age 15 - 18 months)**	24
2	**No. of Study Centers**	02 **Dr. Sharad Agarkhedkar** Dr. D.Y. Patil Medical College, Pune. **Dr. Ram K. Dhongade** Sant Dnyaneshwar Medical Education and Research Centre, Pune.
3	**Study Duration**	2 Months
4	**Study Vaccine**	**EasySix®** , Single Dose, Deep Intramuscular
5	**ADR Observation Period**	6 hours post vaccination and Upto 7 days post-vaccination
6	**Laboratory Tests: Hematological Parameters**	CBC (Complete Blood Count) LFT (Liver Functions Test) KFT (Kidney Function Test)

Safety and Reactogenicity

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Sr. No.	Local Reaction	Grade	N (%)
1	**Pain / Tenderness**	All	14 (58.33)
		Mild	10 (41.67)
		Moderate	4 (16.67)
2	**Swelling**	All	11 (45.83)
		Mild	10 (41.67)
		Moderate	1 (4.17)
3	**Hardness / Induration**	All	7 (29.17)
		Mild	7 (29.17)
		Moderate	0 (0)
4	**Redness / Erythema**	All	6 (25)
		Mild	6 (25)
		Moderate	0 (0)

Reference: Data on File.: EasySix™ Phase I Clinical Study, Data on File, Protocol No: PBL/CR/2010/04/CT, Version:2.0 Dated:05-08-10

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Results & Conclusion

- Majority of Local Reactions were Mild
- EasySix®is found to be Safe and Well Tolerated in all 24 Infants in Phase I trial

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Phase III Trial

Comparative Study

DTwP-Hep B-Hib-IPV vaccine (EasySix®, Panacea Biotec Ltd.)

Versus

Pentavalent (DTwP-Hep B-Hib) (Pentavac ®, Serum Institute)

with IPV (Imovax ®, Sanofi Pasteur)

Publication

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

A randomized, open label trial to evaluate and compare the immunogenicity and safety of a novel liquid hexavalent DTwP-Hib/Hep B-IPV (EasySix™) to licensed combination vaccines in healthy infants

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Phases III Clinical Trial

Study Title

An Open Label, Randomized, Multicenter study to Evaluate and Compare the Immunogenicity and Reactogenicity of **EasySix®** (Fully Liquid Hexavalent DTwP-HepB-Hib-IPV Vaccine, Panacea Biotec Ltd.) with **Pentavac SD®** (Pentavalent DTwP-HepB/Hib Vaccine, Serum Institute of India Pvt. Ltd.) co-administered with **Imovax Polio®** (Salk Based Inactivated Polio Vaccine, Sanofi Pasteur India Pvt. Ltd.) in Healthy Infants.

Aim

To assess and compare the Immunogenicity (primary objective) and Reactogenicity (secondary objective) of Fully liquid Hexavalent **EasySix®** vaccine (DTwP-HepB-Hib-IPV, Panacea Biotec) with **Pentavac SD®** (Pentavalent DTwP-HepB/Hib Vaccine, Serum Institute of India Ltd.) co-administered with **Imovax Polio®** (Sanofi Pasteur India Pvt. Ltd.) in Healthy Infants

Primary Endpoints

Proportion of subjects **achieving seroprotection** against diphtheria, tetanus, Hepatitis B, Hib; seroresponsiveness against pertussis; seroconversion against Polio virus type 1, type 2 and type 3, 4 weeks after three dose vaccination series of DTwP-HepB-Hib-IPV vaccine in the two treatment groups

Secondary Endpoints

- Incidence of solicited local and systemic reactions during 4 days of each vaccine dose (day 0-3).
- Incidence of unsolicited adverse events up to 4 weeks after each vaccination.
- Incidence of SAE during the entire study period.

Immunogenicity: ability to produce immune response;
reactogenicity to produce common, "expected" adverse reactions, associated signs and symptoms—fever, pain, redness etc

Study Design

Design	Open Label, Multi-centric, Randomized, Parallel group, Comparative study (active control).
No. of Study Centers	Four 1. **Dr. Ram Dhongade-** Sant Dnyaneshwar Medical Education Research Centre, Pune 2. **Dr. S. M. Prasad** - Dr B. R. Ambedkar Medical College, Bengaluru 3. **Dr. A. Swamy Naidu-** King George Hospital, Visakhapatnam 4. **Dr J. Venkateswara Rao** - Gandhi Medical College & Hospital, Hyderabad
Indication	Primary immunization against Diphtheria, Pertussis, Tetanus, Hepatitis B, Haemophilus Influenza and Polio
Study Arms	Two
Test	Fully liquid hexavalent DTwP-HepB-Hib-IPV vaccine (EasySix™, Panacea Biotec Ltd.)
Comparator	Pentavalent DTwP- HepB-Hib Vaccine (Pentavac) co-administered with IPV (Salk Based Inactivated Polio Vaccine) (Imovax)
Age Group	6 - 10 weeks (infants)
Enrolled Subjects	**284 (Each arm with 142 Infants).**
Dosage and Administration	0.5 ml of each vaccine administered by deep IM injection in the anterolateral aspect of thigh.
Schedule	6, 10, and 14 weeks.

Reference: A randomized, open label trial to evaluate and compare the immunogenicity and safety of a novel liquid hexavalent DTwP-Hib/Hep B-IPV (EasySix™) to licensed combination vaccines in healthy infants. Vaccine. 2018

Inclusion Criteria

- Infants 6-10 weeks of age, whose parents/LAR willing to give written informed consent prior to the study entry.
- Infants with good health as determined by:
    - Medical history
    - Physical examination
    - Clinical judgment of the investigator
- Judged to be able to attend all scheduled study visits and to comply with trial procedures.

Exclusion Criteria

- Infants weighing < 3.3 Kg at the time of enrollment.
- Infants less than 6 weeks or more than 10 weeks of age.
- Known HBsAg positivity in mother.
- Infants having history of immunization with vaccine other than zero polio, BCG and birth dose of HepB
- Infants with history of infection potentially related to any of the agents targeted by the DPT-HepB-Hib-IPV vaccine
- Presence of evolving or changing neurological disorder or Infants with history of seizures before receiving the vaccine. Initiation or continuation of pertussis vaccination should be deferred until an evolving neurological disorder can be excluded.
- History of household contact and/or intimate exposure to an individual with suspected poliomyelitis.
- Fever >38^{o} C in past 3 days
- Any evidence of acute illness or infection within past 7 days.

Exclusion Criteria

- Planned or elective surgery during the course of the study.
- Infants with a known or suspected impairment of the immune function (congenital or hereditary), or those receiving immunosuppressive therapy, or received immunosuppressive therapy prior to study entry (including systemic or high doses of inhaled corticosteroids) or those who have received a parenteral immunoglobulin preparation
- Infants who have received any blood products, cytotoxic agents or radiotherapy.
- Infants with history of anaphylaxis, or any serious vaccine reaction, or allergy to any vaccine component.
- Have any clinically significant chronic disease (for example, cardiac, pulmonary, renal, gastrointestinal, hepatic, endocrine, cancer, skin or psychiatric disease or disorder or autoimmune disease under treatment) or major congenital defects, such that it would endanger the volunteer's wellbeing or which, in the opinion of the investigator, might interfere with the evaluation of the study objectives.
- Any evidence of thrombocytopenia or a bleeding disorder.
- Infants who have participated in another trial or received an investigational agent within 30 days of enrolment.

EasySix:Comparative Immunogenicity

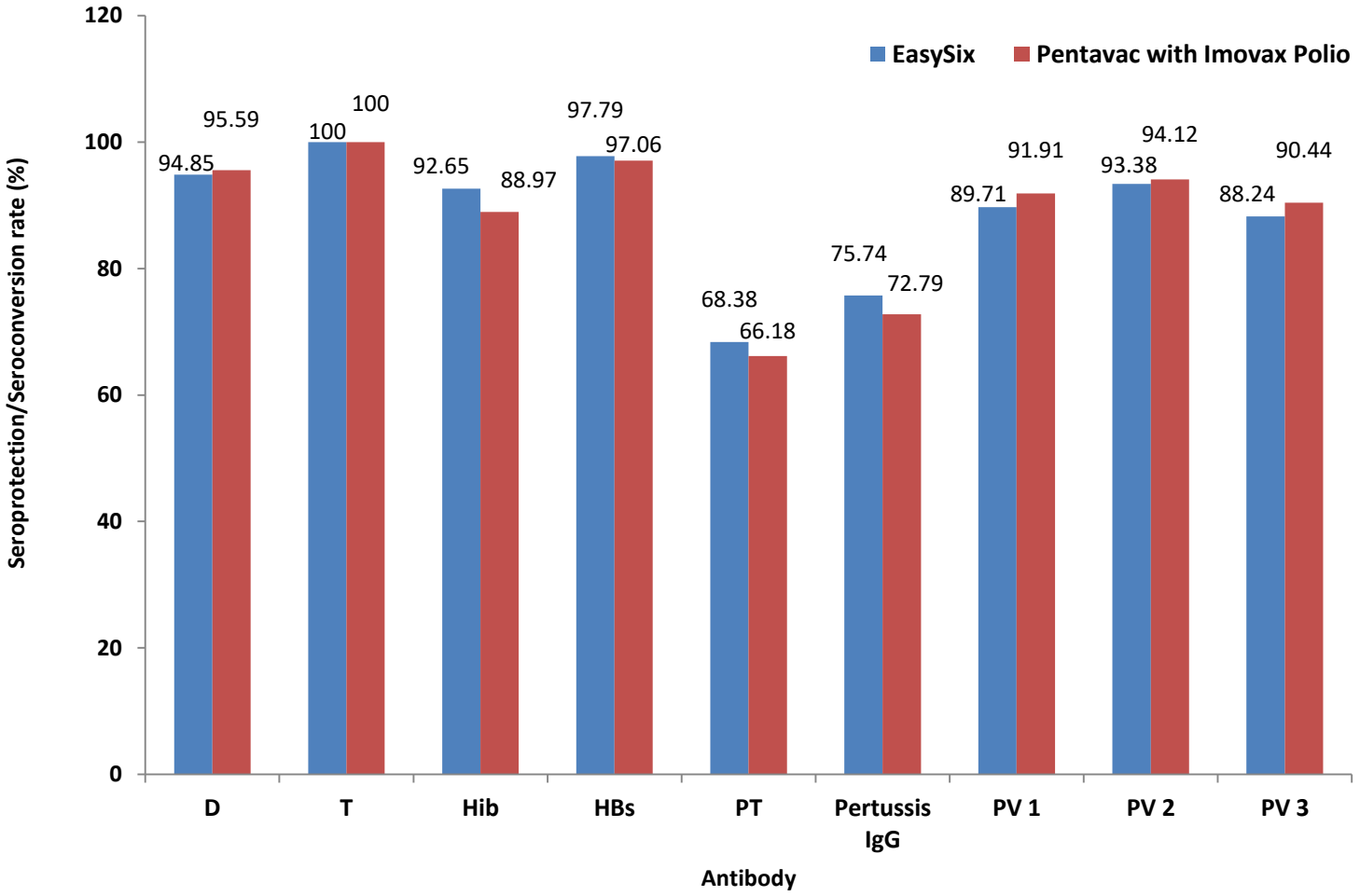
Antigen	EasySix™ (N = 136)	Comparator* (DTwP-Hep B-Hib with IPV) (N = 136)
	N (%)	N (%)
Anti-Diphtheria	129 (94.85)	130 (95.59)
Anti-Tetanus	136 (100)	136 (100)
Anti-PRP (Short term)	136 (100)	136 (100)
Anti-PRP (Long term)	126 (92.65)	121 (88.97)
Anti-HBs	133 (97.79)	132 (97.06)
Anti-PT	93 (68.38)	90 (66.18)
Pertussis IgG	103 (75.74)	99 (72.79)
Anti-Polio Type 1	122 (89.71)	125 (91.91)
Anti-Polio Type 2	127 (93.38)	128 (94.12)
Anti-Polio Type 3	120 (88.24)	123 (90.44)

Seroconversion rate of EasySix against all antigens is comparable with DTwP-Hep B-Hib with IPV

Reference: A randomized, open label trial to evaluate and compare the immunogenicity and safety of a novel liquid hexavalent DTwP-Hib/Hep B-IPV (EasySix™) to licensed combination vaccines in healthy infants. Vaccine. 2018

Seroprotection /Seroconversion Response rate

Easy Six



EasySix Vaccine Exhibited Comparable Immunogenicity

Reference: A randomized, open label trial to evaluate and compare the immunogenicity and safety of a novel liquid hexavalent DTwP-Hib/Hep B-IPV (EasySix™) to licensed combination vaccines in healthy infants. Vaccine. 2018

Antibody GMTs (Immunogenicity Cohorts)

Antibody	Group	Timing	N	GMT		
					95% CI	
				Value	LL	UL
Anti-Diphtheria (IU/ml)	EasySix™	Post Vaccination	136	0.77	0.62	0.96
		Pre Vaccination	136	0.04	0.03	0.05
	Pentavac SD® co-administered with Imovax Polio®	Post Vaccination	136	0.98	0.78	1.22
		Pre Vaccination	136	0.03	0.02	0.04
Anti-Tetanus (IU/ml)	EasySix™	Post Vaccination	136	1.16	1.02	1.31
		Pre Vaccination	136	1.18	1.01	1.38
	Pentavac SD® co-administered with Imovax Polio®	Post Vaccination	136	1.12	1.00	1.25
		Pre Vaccination	136	1.02	0.85	1.23
Anti-PRP (µg/ml)	EasySix™	Post Vaccination	136	12.33	9.29	16.36
		Pre Vaccination	136	0.81	0.67	0.98
	Pentavac SD® co-administered with Imovax Polio®	Post Vaccination	136	8.97	6.87	11.71
		Pre Vaccination	136	0.69	0.58	0.82
Anti-HBs (mIU/ml)	EasySix™	Post Vaccination	136	328.57	214.01	504.44
		Pre Vaccination	136	0.00	0.00	0.01
	Pentavac SD® co-administered with Imovax Polio®	Post Vaccination	136	244.97	150.53	398.68
		Pre Vaccination	136	0.00	0.00	0.02

Antibody GMTs (Immunogenicity Cohorts) (cont.)

Antibody	Group	Timing	N	GMT		
					95% CI	
				Value	LL	UL
Anti-PT (µg/ml)	EasySix™	Post Vaccination	136	45.97	36.29	58.24
		Pre Vaccination	136	4.65	3.59	6.03
	Pentavac SD® co-administered with Imovax Polio®	Post Vaccination	136	47.33	35.82	62.55
		Pre Vaccination	136	3.14	2.02	4.91
Pertussis IgG (IU/ml)	EasySix™	Post Vaccination	136	25.64	23.33	28.18
		Pre Vaccination	136	12.21	10.50	14.21
	Pentavac SD® co-administered with Imovax Polio®	Post Vaccination	136	21.69	19.55	24.07
		Pre Vaccination	136	10.31	8.56	12.42
Anti-Polio Type 1 ≥8 (1/dilution)	EasySix™	Post Vaccination	136	155.92	106.90	227.44
		Pre Vaccination	136	1.00	0.78	1.29
	Pentavac SD® co-administered with Imovax Polio®	Post Vaccination	136	221.05	152.69	320.01
		Pre Vaccination	136	0.79	0.64	0.97
Anti-Polio Type 2 ≥8 (1/dilution)	EasySix™	Post Vaccination	136	243.52	174.07	340.68
		Pre Vaccination	136	1.13	0.87	1.47
	Pentavac SD® co-administered with Imovax Polio®	Post Vaccination	136	354.13	250.05	501.52
		Pre Vaccination	136	0.82	0.66	1.03
Anti-Polio Type 3 ≥8 (1/dilution)	EasySix™	Post Vaccination	136	197.10	131.11	296.31
		Pre Vaccination	136	1.03	0.80	1.33
	Pentavac SD® co-administered with Imovax Polio®	Post Vaccination	136	260.18	173.62	389.91
		Pre Vaccination	136	0.79	0.64	0.99

EasySix®:Safety Results

- No death reported in the trial.
- One SAE (Pneumonia) was reported in the trial: NOT RELATED to the study vaccine.
- Most Systemic solicited and local events were mild/moderate and resolved completely with symptomatic treatment.

EasySix®: Safe & Well tolerated

Adverse Events (AEs)	EasySix N (%)	Comparator * (DTwP - HepB-Hib with IPV) N (%)	
Any AEs	100 (70.42)	106 (74.64)	
Any Unsolicited AEs	1 (0.70)	2 (1.40)	
Any Solicited AEs	99 (69.71)	104 (73.23)	
Any Solicited Local AEs	79 (55.63)	DTwP-Hep B-Hib	IPV
		84 (59.15)	53 (38.02)

- Exhibited Less Pain and Tenderness.
- Comparable Local (redness and swelling) and Systemic (fever and irritability / restlessness / fuzziness) AE's.

Reference: A randomized, open label trial to evaluate and compare the immunogenicity and safety of a novel liquid hexavalent DTwP-Hib/Hep B-IPV (EasySix™) to licensed combination vaccines in healthy infants. Vaccine. 2018

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Conclusion

- World’s first fully liquid wP-based hexavalent vaccine is safe and immunogenic
- Indian NRA approved through phase I and phase III clinical trials.
- Non-inferiority was demonstrated at the level of proportion of infants developing seroprotective titers or showing seroconversion following the primary series of vaccine compared to the same target-antigens included in licensed combination vaccines.
- Has comparable immunogenicity versus DTwP-Hep B-Hib with IPV in 284 Indian infants study.
- Exhibited less pain and tenderness, less local and systemic adverse events, hence well tolerated.
- 6 in 1 wP-based hexavalent vaccine for broad and long term protection.

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Thank You for your kind attention !