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Prescribing decisions should be made based on the approved package insert in the country of prescription.*

Sponsor: Sanofi	Study Identifiers: NCT00674908
Drug substance(s): DTPwHB-Hib combination vaccine (SHAN 5®)	Study code: DTPwHB - Hib/2007/0200
Title of the study: Randomized, Single blind, Multicentric, Comparative, Vaccine Interchangeability trial of SHAN 5® (Liquid) and Easy Five (Liquid) [Diphtheria, Tetanus, Pertussis, Hepatitis B and Hib pentavalent combination Vaccines] in Indian infants	
Study center(s): 3 centers in India	
Study period: Date first subject enrolled: 16/Apr/2008 Date last subject completed: 14/Jan/2009	
Phase of development: Phase IV	
Objectives: The objective of this study was to compare the Safety and Immunogenicity of a mixed sequence of 2 different pentavalent vaccines (Diphtheria - Tetanus - Pertussis, Hepatitis B and <i>Haemophilus influenzae</i> type b (Hib) combination Vaccines) with single sequence of SHAN 5® in infants.	
Methodology: Randomized, Multicentric, Comparative, Prospective, Single blind, intention to treat, vaccine interchangeability trial.	
Number of subjects: Planned: 144 Randomized: 144 Treated: 144	
Evaluated: Immunogenicity: 128 Safety: 144	
Diagnosis and criteria for inclusion: <ul style="list-style-type: none"> • Infants between 6 - 8 weeks of age • Mother's HbsAg assured negative during pregnancy. • Born after a gestational period of 36 – 42 weeks • Father, mother or legally acceptable representative (guardian) properly informed about the study and having signed the informed consent form • Parent/s or guardian of subject willing to maintain diary card. 	

<p>Study treatments</p> <p>Investigational medicinal product: DTPwHB - Hib combination vaccines (SHAN 5[®] and EasyFive)</p> <p>Formulation: Liquid</p> <p>Route of administration: Deep intramuscular injection, preferably in the anterolateral thigh.</p> <p>Dose regimen: Three doses of 0.5 mL each at the age of 4 to 6 weeks, 10 to 12 weeks and 14 to 16 weeks</p>
<p>Duration of treatment: 10 weeks</p> <p>Duration of observation: 30 minutes to 3 hours after each dose</p>
<p>Criteria for evaluation:</p> <p>Immunogenicity:</p> <p>Monitoring the humoral immune response induced by each component i.e. diphtheria, tetanus, pertussis, hepatitis - B and Hib before the first dose and four to six weeks after the last dose of vaccines in all groups</p> <p>Safety:</p> <p>Assessment of adverse events after every dose of vaccine administered</p>
<p>Statistical methods:</p> <p>Descriptive statistics such as number, mean, median, standard deviation and range (minimum, maximum) were used for summarizing the continuous variables. Frequencies and relative frequencies were computed for categorical data. Graphs like histograms, line charts, pie charts, etc were generated wherever necessary.</p> <p>Concentrations of antibodies were log transformed, and geometric mean antibody concentrations (GMCs) compared using analysis of variance (ANOVA). The proportions of participants who responded to each of the vaccine antigens were compared using Chi - square.</p> <p>In addition to traditional statistics, the immunogenicity data was analyzed for non - inferiority. The objective was to rule out that the mixed sequence groups were inferior to the all - SHAN 5[®] group with respect to the immune responses to the vaccine antigens. Analysis of safety was performed on the total vaccinated cohort. The percentages of infants experiencing a symptom within 3 days following vaccination was computed with the exact 95% confidence interval (CI), according to the type and intensity of the symptom and its relationship to vaccine. Occurrence rates of adverse reactions (after each dose and overall for all the three groups and center wise) were compared using Chi - square or Fisher's exact tests. Geometric Mean Antibody Concentrations at preimmunization and post - immunization were compared using paired t - test.</p> <p>All statistical analyses were performed using SAS version 8.2.</p>
<p>Summary:</p> <p>Population characteristics:</p> <p>Overall 144 subjects were recruited at different centers to recruit 48 in the single sequence (SSS) group, 48 in the mixed sequence (SSE) group and 48 in the mixed sequence (SEE) group. Of these subjects 128 were evaluable as per protocol for immunogenicity whereas all 144 were available for safety.</p> <p>Immunogenicity:</p> <p>There was 100% seroconversion for anti diphtheria antibodies in all the three groups. Groups SSS and SSE showed 100% seroconversion for anti tetanus antibodies as compared to 97.78% in SEE group. There was 48.78%, 38.10% and 48.89% seroconversion for pertussis antibodies in the SSS, SSE and SEE groups respectively. Anti hepatitis B antibodies were associated with 97.56%, 97.62% and 100% seroconversion in the SSS, SSE and SEE study groups respectively. SSS, SSE and SEE study groups showed 97.56%, 97.62% and 100% seroconversion for anti PRP antibodies respectively. There were no significant differences in the seroconversion for each of the five components across all the three study groups. There were non significant differences between the post vaccination GMTs for all the three study groups across all five antigens (Anti Diphtheria Toxoid</p>



P=0.8273; Anti Tetanus Toxoid P=0.9604; Anti Pertussis antibody P=0.0537; Anti Hepatitis B antibody P=0.9273; Anti Hib antibody P=0.4442)

Safety results:

Local pain at the site of injection was the most common local Adverse Events Following Immunization (AEFI) across all study groups followed by local swelling. Among the systemic AEFIs, crying after vaccination was most commonly reported, followed by fever. Fever was mostly mild in nature and subsided on its own. Only on one occasion was a fever of $\geq 103^{\circ}\text{F}$ recorded in SSS and SSE groups. There were no Serious Adverse Events (SAEs) reported in the study.

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