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<b>Study No.:</b> 213503/026 (DTPa-IPV-026)
<b>Title:</b> Open, randomized clinical study to assess the reactogenicity and immunogenicity of SB Biologicals' DTPa vaccine co-administered with SB Biologicals' Hib vaccine in two concomitant injections into opposite limbs, as compared to SB Biologicals' DTPa vaccine mixed with SB Biologicals' Hib vaccine and to SB Biologicals' DTPa-IPV vaccine mixed with SB Biologicals' Hib vaccine, administered as a booster dose to healthy children in their second year of life, previously primed with three doses of SB Biologicals' DTPa-HBV-IPV vaccine. <i>Infanrix</i> (DTPa): GlaxoSmithKline (GSK) Biologicals' (previously SmithklineBeecham Biologicals) combined diphtheria, tetanus and acellular pertussis vaccine. Hib: GlaxoSmithKline (GSK) Biologicals' (formerly SmithklineBeecham Biologicals) <i>Haemophilus influenzae</i> type b vaccine. DTPa: GSK Biologicals' combined diphtheria, tetanus and acellular pertussis vaccine. DTPa-HBV-IPV: GSK Biologicals' combined diphtheria, tetanus and acellular pertussis vaccine, recombinant hepatitis B vaccine and inactivated polio vaccine.
<b>Rationale:</b> The purpose of the study was to evaluate the safety and immunogenicity of three different booster vaccination regimen following the primary course given in study DTPa-HBV-IPV-012 (217744/012). <i>Polio Sabin</i> <sup>TM</sup> (OPV): GSK Biologicals' live attenuated oral polio vaccine.
<b>Phase:</b> III
<b>Study Period:</b> 4 March 1997 to 8 July 1997
<b>Study Design:</b> Open, randomized, multicenter study with 3 parallel groups (1:1:1).
<b>Centers:</b> 5 centers in Lithuania.
<b>Indication:</b> Booster vaccination against diphtheria, tetanus, pertussis, <i>Haemophilus influenzae</i> type b disease and poliomyelitis in healthy children in their second year of life.
<b>Treatment:</b> The treatment groups were as follows: <ul style="list-style-type: none"> <li>• DTPa + Hib + OPV Group: received concomitant administration of DTPa vaccine, Hib vaccine as separate injections and OPV vaccine.</li> <li>• DTPa/Hib + OPV Group: received combined DTPa and Hib vaccine with co-administered OPV vaccine.</li> <li>• DTPa-IPV/Hib Group: received combined DTPa-IPV/Hib vaccine.</li> </ul> All the vaccines were administered as a single dose. DTPa, DTPa/Hib and DTPa-IPV/Hib vaccines were administered intramuscularly in the left anterolateral thigh. Hib vaccine was administered intramuscularly in the right anterolateral thigh when administered alone. OPV was administered orally.
<b>Objectives:</b> To evaluate and compare the local reactogenicity of the three booster vaccination regimens.
<b>Primary Outcome/Efficacy Variable:</b> <i>Safety:</i> <ul style="list-style-type: none"> <li>• Incidence and intensity of solicited local reactions (swelling, redness, pain) at the injection site(s) of the study vaccines during the 4-day follow up period after vaccination.</li> </ul>
<b>Secondary Outcome/Efficacy Variable(s):</b> <i>Immunogenicity:</i> Before the booster dose: <ul style="list-style-type: none"> <li>• Anti-diphtheria, anti-tetanus, anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA), anti-pertactin (anti-PRN), anti-polio type 1, 2 &amp; 3 and anti-polyribosyl ribitol phosphate (anti-PRP) antibody concentrations or titers and geometric mean antibody concentration (GMCs) or titers (GMTs). <ul style="list-style-type: none"> <li>- for anti-diphtheria and anti-tetanus: percentage of subjects with concentrations <math>\geq 0.1</math> IU/mL .</li> <li>- for anti-PT, anti-FHA, and anti-PRN: percentage of subjects with concentrations <math>\geq 5</math> EL.U/mL.</li> <li>- for anti-polio 1, 2 &amp; 3: percentage of subjects with titers <math>\geq 8</math></li> </ul> </li> <li>• Anti-PRP <ul style="list-style-type: none"> <li>- percentage of subjects with concentrations <math>\geq 0.15</math> <math>\mu</math>g/mL and <math>\geq 1.0</math> <math>\mu</math>g/mL.</li> </ul> </li> <li>• Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations and GMCs. <ul style="list-style-type: none"> <li>- percentage of subjects with titers <math>\geq 10</math> mIU/mL (only pre-booster vaccination GMCs were available).</li> </ul> </li> </ul> One month after the booster dose: <ul style="list-style-type: none"> <li>• Anti-diphtheria, anti-tetanus, anti-PT, anti-FHA, anti-PRN, anti-polio type 1, 2 &amp; 3 and anti-PRP antibody</li> </ul>

<p>concentrations or titers and geometric mean antibody concentration (GMCs) or titers (GMTs).</p> <ul style="list-style-type: none"> <li>- for anti-diphtheria and anti-tetanus: percentage of subjects with concentrations <math>\geq 0.1</math> IU/mL .</li> <li>- for anti-PT, anti-FHA, and anti-PRN: percentage of subjects with concentrations <math>\geq 5</math> EL.U/mL.</li> <li>- for anti-polio 1, 2 &amp; 3: percentage of subjects with titers <math>\geq 8</math>.</li> </ul> <ul style="list-style-type: none"> <li>• Vaccine response to pertussis antigens: PT, FHA and PRN. Vaccine response is defined as : <ul style="list-style-type: none"> <li>– For initially seronegative subjects, vaccine response is indicated by a post-vaccination antibody concentration <math>\geq 5</math> EL.U/mL.</li> <li>– For initially seropositive subjects, vaccine response is indicated by at least a two-fold increase from pre-vaccination titer to post-vaccination concentration.</li> </ul> </li> <li>• Vaccine response to polio type 1, 2 and 3 antigens. Vaccine response is defined as : <ul style="list-style-type: none"> <li>– For initially seronegative subjects, vaccine response is indicated by a post-vaccination antibody titer <math>\geq 8</math>.</li> <li>– For initially seropositive subjects, vaccine response is indicated by at least a two-fold increase from pre-vaccination titer to post-vaccination titer.</li> </ul> </li> <li>• Anti-PRP <ul style="list-style-type: none"> <li>- percentage of subjects with titers <math>\geq 0.15</math> <math>\mu</math>g/mL and <math>\geq 1.0</math> <math>\mu</math>g/mL.</li> </ul> </li> </ul> <p><b>Safety:</b></p> <ul style="list-style-type: none"> <li>• Incidence, intensity and relationship to vaccination of solicited general symptoms within 48 hours and during the 4-day follow up period after vaccination.</li> <li>• Incidence, nature, intensity and relationship to vaccination of unsolicited adverse events during the 30-day follow-up period after vaccination.</li> <li>• Incidence, nature and relationship to vaccination of serious adverse events during the study period.</li> </ul> <p><b>Statistical Methods:</b> The analysis was performed on the Total Cohort, According to Protocol (ATP) Cohort for immunogenicity and ATP Cohort of safety.</p> <ul style="list-style-type: none"> <li>- The Total Cohort included all subjects enrolled in the study for whom data were available.</li> <li>- The ATP Cohort for immunogenicity included all evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component.</li> <li>- The ATP Cohort for safety included the subjects who received at least one dose of the study vaccine with sufficient data to perform an analysis and abided by the protocol.</li> </ul> <p><b>Analysis of immunogenicity</b> The analyses were performed on the ATP Cohort for immunogenicity and the Total Cohort. For each vaccine antigen, the seroprotection and seropositivity rates and GMCs/GMTs before and one month after vaccination and their exact 95% confidence intervals (CIs) were calculated for each group. The percentages of subjects with booster response to PT, FHA, PRN and poliovirus with their exact 95% CIs were calculated for each group.</p> <p><b>Analysis of safety</b> The analyses were performed on the ATP Cohort for safety. For each solicited symptom, the incidence, intensity and, for general symptom, the relationship to vaccination within 48 hours and during the 4 day follow up period after vaccination were summarized. The incidence, intensity and relationship to vaccination of unsolicited adverse events after vaccination were tabulated according to the World Health Organization's (WHO) Dictionary for Adverse Reaction Terminology. The incidence and relationship to vaccination of serious adverse events during the study period were also tabulated.</p>			
<p><b>Study Population:</b> Healthy children 15 - 24 months of age at the time of the booster vaccination who previously participated in 27744/012 study and completed a three-dose primary vaccination course of DTPa-HBV-IPV and Hib vaccines with no history of previous diphtheria, tetanus, pertussis and/or polio booster vaccination or disease. Written informed consent was obtained from the parents or guardians of the subject prior to study entry.</p>			
<b>Number of Subjects:</b>	<b>DTPa + Hib + OPV Group</b>	<b>DTPa/Hib + OPV Group</b>	<b>DTPa-IPV/Hib Group</b>
Planned, N	110	110	110
Randomized, N	92	92	89
Completed, n (%)	90 (97.8)	92 (100.0)	89 (100.0)
Total Number Subjects Withdrawn, n (%)	2 (2.2)	0 (0.0)	0 (0.0)

Withdrawn due to Adverse Events n (%)	0 (0.0)	0 (0.0)	0 (0.0)				
Withdrawn due to Lack of Efficacy n (%)	Not applicable	Not applicable	Not applicable				
Withdrawn for other reasons n (%)	2 (2.2)	0 (0.0)	0 (0.0)				
<b>Demographics</b>	<b>DTPa + Hib + OPV Group</b>	<b>DTPa/Hib + OPV Group</b>	<b>DTPa-IPV/Hib Group</b>				
N (Total Cohort)	92	92	89				
Females: Males .	36:56	51:41	53:36				
Mean Age, months (SD)	17.4 (1.15)	17.2 (1.52)	17.3 (1.33)				
White/Caucasian, n (%)	92 (100.0)	92 (100.0)	89 (100.0)				
<b>Primary Efficacy Results:</b> Total incidence of all solicited local symptoms and the incidence of solicited local symptoms graded "3" during the 4-day follow-up period after the booster dose (ATP analysis of safety).							
<b>Symptom</b>	<b>Intensity</b>	<b>DTPa + Hib + OPV Group N = 65</b>	<b>DTPa/Hib + OPV Group N = 65</b>	<b>DTPa-IPV/Hib Group N = 63</b>			
<b>Pain</b>	Any	16.9	24.6	41.3			
	Grade 3	0.0	0.0	0.0			
<b>Redness</b>	Any	63.1	55.4	73.0			
	>20 mm	16.9	27.7	41.3			
<b>Swelling</b>	Any	44.6	40.0	55.6			
	>20 mm	18.5	24.6	31.7			
N = total number of doses administered with a symptom sheet returned (i.e. documented doses) % = percentage of subjects reporting the specified solicited local symptom Any = any specified symptoms reported during the follow-up period Grade 3 pain: pain prevented everyday activities							
<b>Secondary Outcome Variable(s):</b> Total incidence of all solicited general symptoms, the incidence of solicited general symptoms with an onset within 2 days of vaccination, the incidence of solicited general symptoms graded "3" and those considered to have relationship to vaccination during the 4-day follow-up period after the booster dose (ATP analysis of safety).							
<b>Symptom</b>	<b>Intensity/Relationship</b>	<b>DTPa + Hib + OPV Group N = 65</b>		<b>DTPa/Hib + OPV Group N = 65</b>		<b>DTPa-IPV/Hib Group N = 63</b>	
		<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>
<b>Diarrhea</b>	Any	5	7.7	7	10.8	7	11.1
	Grade 3	0	0.0	1	1.5	0	0.0
	Related	4	6.2	7	10.8	7	11.1
<b>Fever</b>	Any	5	7.7	3	4.6	9	14.3
	Grade 3	0	0.0	0	0.0	2	3.2
	Related	4	6.2	3	4.6	6	9.5
<b>Loss of appetite</b>	Any	14	21.5	8	12.3	21	33.3
	Grade 3	0	0.0	0	0.0	1	1.6
	Related	13	20.0	7	10.8	19	30.2
<b>Sleeping less than usual</b>	Any	20	30.8	17	26.2	18	28.6
	Grade 3	1	1.5	0	0.0	2	3.2
	Related	18	27.7	15	23.1	16	25.4
<b>Unusual crying</b>	Any	12	18.5	15	23.1	14	22.2
	Grade 3	0	0.0	0	0.0	1	1.6
	Related	10	15.4	15	23.1	13	20.6
<b>Vomiting</b>	Any	0	0.0	0	0.0	3	4.8
	Grade 3	0	0.0	0	0.0	0	0.0
	Related	0	0.0	0	0.0	3	4.8
Grade 3 symptom = symptom preventing everyday activity Any fever = axillary/oral temperatures $\geq 37.5^{\circ}\text{C}$ or rectal temperatures $\geq 38.0^{\circ}\text{C}$ Grade 3 fever = Fever $\geq 39.1^{\circ}\text{C}$ (axillary/oral) or $\geq 39.6^{\circ}\text{C}$ (rectal) N = total number of doses administered with a symptom sheet returned (i.e. documented doses)							

n (%) = total number (percentage) of documented doses followed by the specific symptom  
 Any = any specified symptoms reported during the follow-up period  
 Onset 2 days = all specified symptoms with an onset on Day 0, 1 or 2  
 Related = any symptom 'suspected to be related' or 'probably related' to vaccination

**Secondary Outcome Variable(s):** Seropositivity rates (%) and GMCs of anti-diphtheria antibodies (ATP analysis of immunogenicity).

Group	Timing	N	S+		95%CI		GMC (IU/mL)	95% CI	
			n	%	LL	UL		LL	UL
DTPa + Hib + OPV	Pre	60	39	65.0	52.1	77.9	0.146	0.114	0.185
	Post	60	60	100.0	92.5	100.0	5.415	4.296	6.825
DTPa/Hib + OPV	Pre	61	35	57.4	44.1	70.6	0.140	0.106	0.185
	Post	61	61	100.0	92.6	100.0	3.901	3.036	5.013
DTPa-IPV/Hib	Pre	59	35	59.3	45.9	72.7	0.142	0.110	0.185
	Post	60	60	100.0	92.5	100.0	5.021	3.901	6.461

Pre = pre-booster  
 Post = approximately one month after the booster dose,  
 S+ = concentrations  $\geq 0.1$  IU/mL  
 N = total number of subjects tested  
 n (%) = number (percentage) of subjects with concentrations  $\geq 0.1$  IU/mL  
 95% CI, LL and UL = 95% Confidence Interval, Lower and Upper limits

**Secondary Outcome Variable(s):** Seropositivity rates (%) and GMCs of anti-tetanus antibodies (ATP analysis of immunogenicity).

Group	Timing	N	S+		95% CI		GMC (IU/mL)	95% CI	
			n	%	LL	UL		LL	UL
DTPa + Hib + OPV	Pre	60	57	95.0	85.2	98.7	0.397	0.321	0.491
	Post	60	60	100.0	92.5	100.0	10.872	8.802	13.429
DTPa/Hib + OPV	Pre	62	57	91.9	81.5	97.0	0.365	0.288	0.464
	Post	62	62	100.0	92.7	100.0	7.760	6.379	9.439
DTPa-IPV/Hib	Pre	60	54	90.0	78.8	95.9	0.333	0.264	0.421
	Post	60	60	100.0	92.5	100.0	8.981	7.530	10.711

Pre = pre-booster  
 Post = approximately one month after the booster dose,  
 S+ = concentrations  $\geq 0.1$  IU/mL  
 N = total number of subjects tested  
 n (%) = number (percentage) of subjects with concentrations  $\geq 0.1$  IU/mL  
 95% CI, LL and UL = 95% Confidence Interval, Lower and Upper limits

**Secondary Outcome Variable(s):** Booster vaccine response: Pertussis antigens (ATP analysis of immunogenicity).

Antibody	Group	Pre-vaccination status	N	n	Vaccine Response % [95% CI]
Anti-PT	DTPa + Hib + OPV	S-	8	8	100.0
		S+	52	51	98.1
		Total	60	59	98.3
					[89.9 , 99.9]
	DTPa/Hib + OPV	S-	6	6	100.0
		S+	56	54	96.4
		Total	62	60	96.8
					[87.8 , 99.4]
	DTPa-IPV/Hib	S-	8	8	100.0
		S+	52	51	98.1
		Total	60	59	98.3
					[89.9 , 99.9]
Anti-FHA	DTPa + Hib + OPV	S+	57	54	95.0
		Total	57	54	95.0

	DTPa/Hib + OPV	S-	1	1	[84.5 , 98.6]
		S+	60	57	100.0
		Total	61	58	95.0
					[85.4 , 98.7]
	DTPa-IPV/Hib	S+	60	59	98.3
		Total	60	59	98.3
				[89.9 , 99.9]	
<b>Anti-PRN</b>	DTPa + Hib + OPV	S-	3	3	100.0
		S+	57	54	94.7
		Total	60	57	95.0
					[85.2 , 98.7]
	DTPa/Hib + OPV	S-	3	3	100.0
		S+	59	56	94.9
		Total	62	59	95.2
					[85.6 , 98.7]
	DTPa-IPV/Hib	S-	4	4	100.0
		S+	56	56	100.0
		Total	60	60	100.0
					[92.5 , 100.0]

N = total number of subjects tested  
n = number of subjects with a vaccine response  
95% CI = 95% Confidence Interval  
S+ = concentrations  $\geq 5$  EL.U/mL, S- = concentrations  $< 5$  EL.U/mL  
Vaccine response definition:

For pre-booster seronegative subjects (S-): Appearance of concentrations ( $\geq 5$  EL.U/mL)  
For pre-booster seropositive subjects (S+): At least two-fold increase in pre-vaccination titer

**Secondary Outcome Variable(s):** Seropositivity rates (%) and GMCs of anti-PT, anti-FHA and anti-PRN antibodies (ATP analysis of immunogenicity).

Antibody	Group	Timing	N	S+		95% CI		GMC (EL.U/mL)	95% CI	
				n	%	LL	UL		LL	UL
<b>Anti-PT</b>	DTPa + Hib + OPV	Pre	60	52	86.7	74.9	93.7	10.8	8.7	13.4
		Post	60	60	100.0	92.5	100.0	127.3	108.4	149.6
	DTPa/Hib + OPV	Pre	62	56	90.3	79.5	96.0	12.4	9.9	15.6
		Post	62	62	100.0	92.7	100.0	123.4	103.9	146.5
	DTPa-IPV/Hib	Pre	60	52	86.7	74.9	93.7	10.6	8.4	13.5
		Post	60	60	100.0	92.5	100.0	160.1	132.7	193.2
<b>Anti-FHA</b>	DTPa + Hib + OPV	Pre	57	57	100.0	92.1	100.0	40.1	30.0	53.5
		Post	60	60	100.0	92.5	100.0	597.4	483.4	738.2
	DTPa/Hib + OPV	Pre	61	60	98.4	90.0	99.9	41.6	31.1	55.5
		Post	62	62	100.0	92.7	100.0	593.4	472.9	744.8
	DTPa-IPV/Hib	Pre	60	60	100.0	92.5	100.0	35.2	27.8	44.5
		Post	60	60	100.0	92.5	100.0	558.8	469.9	664.5
<b>Anti-PRN</b>	DTPa + Hib + OPV	Pre	60	57	95.0	85.2	98.7	26.7	20.5	34.9
		Post	60	60	100.0	92.5	100.0	814.9	634.5	1046.6
	DTPa/Hib + OPV	Pre	62	59	95.2	85.6	98.7	24.9	18.1	34.3
		Post	62	62	100.0	92.7	100.0	643.3	512.7	807.1
	DTPa-IPV/Hib	Pre	60	56	93.3	83.0	97.8	18.0	14.0	23.2
		Post	60	60	100.0	92.5	100.0	749.9	604.8	929.8

Pre = pre-booster vaccination  
Post = approximately one month after the booster dose  
S+ = concentrations  $\geq 5$  EL.U/mL

N = total number of subjects tested  
n (%) = number (percentage) of subjects with concentrations  $\geq 5$  EL.U/mL  
95% CI, LL and UL = 95% Confidence Interval, Lower and Upper limits

**Secondary Outcome Variable(s):** Vaccine response to poliovirus (ATP analysis of immunogenicity).

Antibody	Group	Pre-vaccination status	N	n	Vaccine Response %	95% CI [LL;UL]
Anti-polio 1	DTPa + Hib + OPV	S-	1	1	100.0	[83.1 , 98.5]
		S+	51	48	94.1	
		Total	52	49	94.2	
	DTPa/Hib + OPV	S-	1	1	100.0	[79.9 , 97.4]
		S+	49	45	91.8	
		Total	50	46	92.0	
	DTPa-IPV/Hib	S-	1	1	100.0	[87.3 , 99.9]
		S+	46	45	97.8	
		Total	47	46	97.9	
Anti-polio 2	DTPa + Hib + OPV	S+	52	52	100.0	[91.4, 100.0]
		Total	52	52	100.0	
	DTPa/Hib + OPV	S-	1	1	100.0	[85.1 , 99.3]
		S+	49	47	96.0	
		Total	50	48	96.0	
	DTPa-IPV/Hib	S-	1	1	100.0	[90.6 , 100.0]
		S+	46	46	100.0	
		Total	47	47	100.0	
	Anti-polio 3	DTPa + Hib + OPV	S-	2	2	100.0
S+			50	46	92.0	
Total			52	48	92.3	
DTPa/Hib + OPV		S-	1	1	100.0	[65.2, 89.3]
		S+	48	38	79.2	
		Total	49	39	79.6	
DTPa-IPV/Hib		S+	47	46	97.9	[87.3 , 99.9]
		Total	47	46	97.9	

N = total number of subjects tested  
n = number of subjects with a vaccine response  
Vaccine response definition:  
For pre-booster seronegative subjects (S-): Appearance of titer ( $\geq 8$ )  
For post-booster seropositive subjects (S+): At least two-fold increase in pre-vaccination titer  
95% CI, [LL ; UL] = 95% Confidence Interval, [Lower limit ; Upper limit]

**Secondary Outcome Variable(s):** Seropositivity rates (%) and GMTs of anti-polio antibodies (ATP analysis of immunogenicity).

Antibody	Group	Timing	N	S+		95% CI		GMT	95% CI	
				n	%	LL	UL		LL	UL
Anti-polio 1	DTPa + Hib + OPV	Pre	56	54	96.4	86.6	99.4	67.5	50.3	90.5
		Post	56	56	100.0	92.0	100.0	1658.0	1183.4	2323.0
	DTPa/Hib + OPV	Pre	56	55	98.2	89.2	99.9	67.0	50.2	89.5
		Post	56	56	100.0	92.0	100.0	1764.3	1182.7	2631.9
	DTPa-IPV/Hib	Pre	52	50	96.2	85.7	99.3	63.6	44.6	90.6
		Post	55	55	100.0	91.9	100.0	2335.4	1778.4	3066.9
Anti-polio 2	DTPa + Hib + OPV	Pre	56	56	100.0	92.0	100.0	76.4	59.5	98.0
		Post	56	56	100.0	92.0	100.0	5681.2	4579.2	7048.3
	DTPa/Hib + OPV	Pre	56	55	98.2	89.2	99.9	67.1	46.6	96.6

		Post	56	56	100.0	92.0	100.0	6311.2	5369.2	7418.4
	DTPa-IPV/Hib	Pre	52	51	98.1	88.4	99.9	62.6	46.1	85.0
		Post	55	55	100.0	91.9	100.0	3257.9	2606.6	4072.1
Anti-polio 3	DTPa + Hib + OPV	Pre	56	54	96.4	86.6	99.4	113.0	81.7	156.2
		Post	55	55	100.0	91.9	100.0	2471.9	1668.6	3662.1
	DTPa/Hib + OPV	Pre	55	54	98.2	89.0	99.9	152.6	98.4	236.6
		Post	56	55	98.2	89.2	99.9	2330.7	1497.8	3626.8
	DTPa-IPV/Hib	Pre	52	52	100.0	91.4	100.0	150.0	104.4	215.5
		Post	55	55	100.0	91.9	100.0	5099.2	4061.0	6402.7

S+= titers  $\geq$  8

N = total number of subjects tested

n (%) = number (percentage) of subjects with titers  $\geq$  8

Pre = pre-booster vaccination

Post = approximately one month after the booster dose

95% CI, LL and UL = 95% Confidence Interval, Lower and Upper limits

**Secondary Outcome Variable(s):** GMCs and distribution of anti-PRP antibodies concentrations (ATP analysis of immunogenicity).

Group	Timing	N	$\geq 0.15$ $\mu\text{g/mL}$		95% CI		$\geq 1.0$ $\mu\text{g/mL}$		95% CI		GMC ( $\mu\text{g/mL}$ )	95% CI	
			n*	%	LL	UL	n**	%	LL	UL		LL	UL
DTPa + Hib + OPV	Pre	60	56	93.3	83.0	97.8	19	31.7	19.1	44.3	0.731	0.524	1.021
	Post	60	60	100.0	92.5	100.0	60	100.0	92.5	100.0	80.022	59.382	107.83
DTPa/Hib + OPV	Pre	62	56	90.3	79.5	96.0	24	38.7	25.8	51.6	0.857	0.586	1.252
	Post	62	62	100.0	92.7	100.0	61	98.4	90.2	99.9	41.131	30.247	55.933
DTPa-IPV/Hib	Pre	60	54	90.0	78.8	95.9	30	50.0	36.5	63.5	0.819	0.592	1.132
	Post	60	60	100.0	92.5	100.0	60	100.0	92.5	100.0	56.757	43.550	73.969

Pre = pre-booster vaccination, Post = approximately one month after the booster dose

N = total number of subjects tested

n\* (%) = total number (percentage) of subjects with concentrations  $\geq 0.15$   $\mu\text{g/mL}$

n\*\* (%) = total number (percentage) of subjects with concentrations  $\geq 1.0$   $\mu\text{g/mL}$

95% CI, LL and UL = 95% Confidence Interval, Lower and Upper limits

**Secondary Outcome Variable(s):** Pre-booster vaccination GMCs (mIU/mL) for anti-HBs (ATP analysis of immunogenicity).

Antibody	Pre-booster* GMCs**		
	DTPa+Hib+OPV Group	DTPa/Hib + OPV Group	DTPa-IPV/Hib Group
Anti-HBs	346.9	278.8	215.6

\* Only Pre-booster vaccination GMCs were available

\*\* Only subjects with available results were included in the GMC calculations.

**Secondary Outcome Variable(s):** Number of subjects with anti-HBs antibody concentration  $\geq 10$  mIU/mL (ATP analysis of immunogenicity).

Group	Timing	N	$\geq 10$ mIU/mL	
			n	%
DTPa+Hib+OPV	Pre	60	60	100
DTPa/Hib + OPV	Pre	62	61	98.4
DTPa-IPV/Hib	Pre	60	57	95.0

Pre = pre-booster vaccination

N = total number of subjects tested

n (%) = total number (percentage) of subjects with concentrations  $\geq 10$  mIU/mL

**Safety Results:** Number of doses followed by at least one report of unsolicited signs and symptoms classified by WHO Preferred Terms, during the 30-day follow-up period after vaccination (ATP analysis of safety).

Most frequent adverse events - On-Therapy (occurring within Day 0-30 following vaccination)	DTPa+Hib+OPV Group N = 65	DTPa/Hib + OPV Group N = 65	DTPa-IPV/Hib Group N = 63
Subjects with any AE(s), n (%)	11(16.9)	15 (23.1)	17 (27.0)

Subjects with Grade 3 AE(s), n (%)	0 (0.0)	1 (1.6)	0 (0.0)
Subjects with related AE(s), n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis contact	0 (0.0)	1 (1.6)	-
Allergic reaction	0 (0.0)	0 (0.0)	1(1.6)
Injury	0 (0.0)	0 (0.0)	1(1.6)
Dyspepsia	1(1.6)	0 (0.0)	-
Enteritis	1(1.6)	0 (0.0)	-
Gastritis	1(1.6)	0 (0.0)	-
Stomatitis aphthous	0 (0.0)	0 (0.0)	1(1.6)
Tooth ache	0 (0.0)	0 (0.0)	1(1.6)
Balanoposthitis	0 (0.0)	1 (1.6)	-
Upper respiratory tract infection	3(4.6)	2(3.1)	1(1.6)
Bronchitis	0 (0.0)	2(3.1)	1(1.6)
Laryngitis	0 (0.0)	2(3.1)	2(3.2)
Pharyngitis	2 (3.1)	6(9.2)	7(11.1)
Rhinitis	0 (0.0)	1 (1.6)	-
Dermatitis	3(4.6)	0 (0.0)	-
Conjunctivitis	0 (0.0)	0 (0.0)	1(1.6)
Lymphadenopathy	0 (0.0)	0 (0.0)	1(1.6)

Grade 3 AE: AE that prevented normal activities

Related AE: assessed by the investigator as related or possibly related to vaccination

-: Adverse Events absent or not meeting the counting rules

More than 30 subjects/treatment group and > 3 groups: the most frequent 5 events in each treatment group

**Safety results:** Number (%) of subjects with serious adverse events during the 30-day follow-up period after vaccination (ATP analysis of safety).

**Serious adverse event, n (%) [n considered by the investigator to be related to study medication]**

All SAEs	DTPa+Hib+OPV Group N = 65	DTPa/Hib + OPV Group N = 65	DTPa-IPV/Hib Group N = 63
Subjects with any SAE(s), n (%) [n related]	0(0.0)[0]	1(1.6)[0]	1(1.6) [0]
Acute Vial Respiratory	0(0.0)[0]	1(1.6)[0]	0(0.0)[0]
Obstructive Bronchitis	0(0.0)[0]	0(0.0)[0]	1(1.6) [0]
One subject from DTPa+Hib+OPV Group had SAE 39 days after vaccination (Acute Gastroenterocolitis). It was not included in this table.			
Fatal SAEs	DTPa+Hib+OPV Group N = 65	DTPa/Hib + OPV Group N = 65	DTPa-IPV/Hib Group N = 63
Subjects with fatal SAE(s), n (%) [n related]	0(0.0)[0]	0(0.0)[0]	0(0.0)[0]

**Conclusion:**

Following vaccination, 16.9%, 63.1% and 44.6% of the subjects in DTPa+Hib+OPV Group; 24.6%, 55.4% and 40.0% of the subjects in DTPa/Hib + OPV Group and 41.3%, 73.0% and 55.6% of the subjects in DTPa-IPV/Hib Group reported pain, redness and swelling respectively during the 4-day follow-up period. At least one unsolicited symptom during the 30-day follow-up period after vaccination was reported by 11 subjects in DTPa+Hib+OPV Group, 15 subjects in DTPa/Hib + OPV Group and 17 subjects in DTPa-IPV/Hib Group. At least one SAE was reported by 1 subject in DTPa/Hib + OPV Group and 1 subject in DTPa-IPV/Hib Group. No fatal SAEs were reported.

**Publications:** None.

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