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<p><b>Study No.:</b> 106672 (Hib-MenC-TT-022 EXT 010 M18), 106673 (Hib-MenC-TT-023 EXT 010 M30) &amp; 106675 (Hib-MenC-TT-024 EXT 010 M42)</p>
<p><b>Title:</b> A Phase III, open, multicenter study to assess the long-term persistence of a booster dose of GlaxoSmithKline (GSK) Biologicals' <i>Haemophilus influenzae</i> type b-meningococcal serogroup C conjugate vaccine (Hib-MenC) compared to a booster dose of Infanrix™ hexa (combined diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated polio-Hib vaccine) when given to 14-month-old subjects who were primed in study 217744/097 (DTPa-HBV-IPV-097) and boosted in study Hib-MenC-TT-010 BST: DTPa-HBV-IPV-097. Hib-MenC (<i>Menitor</i>™): GSK Biologicals' combined <i>Haemophilus influenzae</i> type b (Hib) and meningococcal serogroup C tetanus toxoid conjugate vaccine DTPa-HBV-IPV/Hib (<i>Infanrix</i>™ hexa): GSK Biologicals' combined diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated polio vaccine and <i>Haemophilus influenzae</i> type b vaccine</p>
<p><b>Rationale:</b> The purpose of this study was to assess the long-term persistence antibodies of a booster dose of Hib-MenC vaccine in subjects primed with either Hib-MenC co-administered with DTPa-HBV and IPV vaccine or with a licensed MenC-TT vaccine co-administered with Hib vaccine reconstituted with a DTPa containing vaccine, compared to a booster dose of DTPa-HBV-IPV/Hib vaccine in subjects primed with a licensed MenC-CRM197 vaccine co-administered with DTPa-HBV-IPV/Hib. DTPa-HBV and IPV: GSK Biologicals' combined diphtheria, tetanus, acellular pertussis, hepatitis B and inactivated polio vaccine MenC-TT vaccine (<i>NeisVac-C</i>™) Baxter's meningococcal C conjugate vaccine MenC-CRM197 vaccine (<i>Meningitec</i>™) Wyeth's meningococcal C conjugate vaccine</p>
<p><b>Phase:</b> III</p>
<p><b>Study Period:</b> 106672: 15 May 2006 to 28 July 2006 106673: 08 May 2007 to 27 September 2007 106675: 22 May 2008 to 06 October 2008</p>
<p><b>Study Design:</b> Open, multicentre study with 3 parallel groups.</p>
<p><b>Centers:</b> 12 centers in Spain</p>
<p><b>Indication:</b> Immunization against Hib and meningococcal C diseases.</p>
<p><b>Treatment:</b> The treatment groups were the same as in the booster study:</p> <ul style="list-style-type: none"> <li>• HibMenC group: primed with Hib-MenC (co-administered with DTPa-HBV and IPV), boosted with Hib-MenC between 13 and 14 months of age.</li> <li>• NeisPoo group: primed with 2 doses of MenC-TT at 2, 4 months of age (co-administered with DTPa-HBV-IPV/Hib at 2, 4, 6 months of age; or co-administered with DTPa-HBV-IPV/Hib at 2, 6 months of age and with DTPa-IPV/Hib at 4 months of age), boosted with Hib-MenC between 13 and 14 months of age</li> <li>• MenCCRM group: primed with MenC-CRM197 vaccine (co-administered with DTPa-HBV-IPV/Hib), boosted with DTPa-HBV-IPV/Hib between 13 and 14 months of age.</li> </ul> <p>To analyse the post-booster data, subjects boosted with Hib-MenC were pooled across primary vaccination schedules into HibCPoo Group (Hib-MenC and NeisPoo groups).</p>
<p><b>Objectives:</b></p> <ul style="list-style-type: none"> <li>• To evaluate the persistence of meningococcal C antibodies on a yearly basis for a period of 5.5 years after booster vaccination.</li> <li>• To evaluate the persistence of <i>Haemophilus influenzae</i> type b antibodies on a yearly basis for a period of 5.5 years after booster vaccination.</li> </ul>
<p><b>Primary Outcome/Efficacy Variable:</b> <i>Immunogenicity</i> At the start of this persistence study and 12 and 24 months later, in all subjects:</p> <ul style="list-style-type: none"> <li>• Meningococcal C serum bactericidal assay using rabbit complement (rSBA-MenC) titers <math>\geq 1:8</math>, <math>\geq 1:32</math>, <math>\geq 1:128</math> and titers.</li> <li>• Anti-polyribosylribitol phosphate (anti-PRP) antibody concentration <math>\geq 0.15 \mu\text{g/mL}</math>, <math>\geq 1 \mu\text{g/mL}</math> and concentrations.</li> <li>• Anti-polysaccharide C (anti-PSC) antibody concentration <math>\geq 0.30 \mu\text{g/mL}</math>, <math>\geq 2.0 \mu\text{g/mL}</math> and concentrations.</li> </ul> <p><i>Safety</i></p>

<ul style="list-style-type: none"> <li>Serious Adverse Events* (SAEs) occurring from the last study contact of the booster study to the end of this persistence study.</li> </ul> <p>*Note: During this long-term persistence study, the subject's parents/guardians were asked retrospectively if any SAE had occurred since the last visit of the booster vaccination study Hib-MenC-TT-010 BST: DTPa-HBV-IPV-097. Only those SAEs that were determined by the investigator to have a causal relationship to the vaccination were described individually in the study report, along with the nature of the SAEs and the outcome.</p>				
<p><b>Secondary Outcome/Efficacy Variable(s):</b> Outcome variables were not differentiated into primary and secondary in study protocol. Hence, all were considered as primary outcome variables.</p>				
<p><b>Statistical Methods:</b> The analyses were performed on the Total vaccinated Cohort, Total cohort Year 1, Total cohort Year 2, Total cohort Year 3 and the According-To-Protocol (ATP) cohort for antibody persistence.</p> <ul style="list-style-type: none"> <li>The Total vaccinated cohort included all subjects who received the booster dose during study 102547 (Hib-MenC-TT-010)</li> <li>The Total cohort Year 1 included all vaccinated subjects in the booster study who came back for the Year 1 follow-up.</li> <li>The Total cohort Year 2 included all vaccinated subjects in the booster study who came back for the Year 2 follow-up.</li> <li>The Total cohort Year 3 included all vaccinated subjects in the booster study who came back for the Year 3 follow-up.</li> <li>The ATP cohort for antibody persistence included all subjects with evaluable data at each time point who received the 3 doses of vaccines according to their random assignment during the primary study and the corresponding booster doses in the booster study, who complied with the procedures defined in the protocol, who had available assay results for one tested antigen at least, who had not received a previous administration of a booster dose of Hib, meningococcal serogroup C vaccines except study vaccines received during the booster study Hib-MenC-TT-010 BST: DTPa-HBV-IPV-097 and who did not have a history of <i>Haemophilus influenzae type b</i>, meningococcal serogroup C diseases.</li> </ul> <p><i>Analysis of immunogenicity.</i> The analysis of immunogenicity was performed on the ATP cohort for antibody persistence. Geometric Mean Concentrations or Titers (GMCs or GMTs) with 95% confidence intervals (CIs) were tabulated for anti-PRP, rSBA-MenC and anti-PSC antibodies; seropositivity rates and percentages of subjects with titers or concentrations above specified cut-offs with exact 95% CIs were calculated for anti-PRP, rSBA-MenC and anti-PSC antibodies.</p> <p><i>Analysis of safety.</i> The analysis of safety was performed on the Total Cohort Year 1, the Total Cohort Year 2 and the Total Cohort Year 3. The SAEs retrospectively reported since the last visit of the booster vaccination study and assessed by the investigator as causally related to the study vaccination were tabulated according to the Medical Dictionary of Regulatory Activities (MedDRA) preferred terms.</p>				
<p><b>Study Population:</b> Male or female subjects in their third year of life for study 106672 (fourth year of life for study 106673 and fifth year of life for study 106675), free of obvious health problems as established by medical history and clinical examination before entering into the study and having completed the booster study Hib-MenC-TT-010 BST: DTPa-HBV-IPV-097 were enrolled in the long-term follow-up study. Written informed consent was obtained from the parent or guardian of the subject prior to study entry.</p>				
<b>Number of Subjects in booster study 102547:</b>	<b>HibMenC Group</b>	<b>NeisPoo Group</b>	<b>HibCPoo Group</b>	<b>MenCCRM Group*</b>
Planned, N	117	234	351	117
Entered, N (Total Vaccinated Cohort)	87	178	265	93
Completed, n (%)	87 (100)	178 (100)	265 (100)	92 (98.9)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	0 (0.0)	(0.0)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)
<b>Demographics</b>	<b>HibMenC Group</b>	<b>NeisPoo Group</b>	<b>HibCPoo Group</b>	<b>MenCCRM Group</b>
N (Total Vaccinated Cohort)	87	178	265	93
Females:Males	45:42	83:95	128:137	49:44
Mean Age, months (SD)	13.3 (0.50)	13.4 (0.54)	13.4 (0.53)	13.3 (0.49)
White/Caucasian, n (%)	71 (81.6)	162 (91.0)	233 (87.9)	83 (89.2)

<b>Number of subjects (Month 18)</b>	<b>HibMenC Group</b>	<b>NeisPoo Group</b>	<b>HibCPoo Group</b>	<b>MenCCRM Group</b>
Planned, N	87	178	265	93
Randomised, N (Total cohort Year 1)	58	123	181	3
Completed, n (%)	58 (100)	123 (100)	181 (100)	3 (100)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Demographics</b>	<b>HibMenC Group</b>	<b>NeisPoo Group</b>	<b>HibCPoo Group</b>	<b>MenCCRM Group</b>
N (Total cohort Year 1)	58	123	181	3
Females:Males	27:31	55:68	82:99	1:2
Mean Age, months (SD)	31.3 (0.54)	31.4 (0.64)	31.3 (0.61)	31.3 (0.58)
White/Caucasian, n (%)	49 (84.5)	112 (91.1)	161 (89.0)	3 (100)
<b>Number of subjects (Month 30)</b>	<b>HibMenC Group</b>	<b>NeisPoo Group</b>	<b>HibCPoo Group</b>	<b>MenCCRM Group</b>
Planned, N	87	178	265	93
Randomised, N (Total Cohort Year 2)	54	119	173	57
Completed, n (%)	54 (100)	119 (100)	173 (100)	57 (100)
Total Number Subjects Withdrawn, n (%)	NA	NA	NA	NA
<b>Demographics</b>	<b>HibMenC Group</b>	<b>NeisPoo Group</b>	<b>HibCPoo Group</b>	<b>MenCCRM Group</b>
N (Total Cohort Year 2)	54	119	173	57
Females:Males	26:28	51:68	77:96	27:30
Mean Age, months (SD)	43.2 (0.80)	43.3 (0.78)	43.3 (0.78)	43.5 (0.87)
White/Caucasian, n (%)	46 (85.2)	108 (90.8)	154 (89.0)	54 (94.7)
<b>Number of subjects (Month 42)</b>	<b>HibMenC Group</b>	<b>NeisPoo Group</b>	<b>HibCPoo Group</b>	<b>MenCCRM Group</b>
Planned, N	58	123	180	92
Randomised, N (Total cohort Year 3)	51	113	164	56
Completed, n (%)	51 (100)	113 (100)	164 (100)	56 (100)
Total Number Subjects Withdrawn, n (%)	NA	NA	NA	NA
<b>Demographics</b>	<b>HibMenC Group</b>	<b>NeisPoo Group</b>	<b>HibCPoo Group</b>	<b>MenCCRM Group</b>
N (Total cohort Year 3)	51	113	164	56
Females:Males	24:27	50:63	74:90	27:29
Mean Age, months (SD)	55.6 (0.83)	55.6 (0.81)	55.6 (0.82)	55.8 (0.89)
White/Caucasian, n (%)	43 (84.3)	103 (91.2)	146 (89.0)	53 (94.6)

\*Subjects from the MenCCRM Group were primed with MenC-CRM197 conjugate vaccine and received a booster dose of the same vaccine outside of the scope of the booster study; therefore they were either not enrolled or eliminated from analyses for Month 18 assessment (Year 1 long-term persistence study, 106672).

A booster dose of a meningococcal serogroup C conjugate vaccine is now being recommended after primary vaccination in infancy in Spain in the framework of the national vaccination schedule. It is thus of interest to evaluate the long-term persistence of SBA-MenC, anti-PSC and anti-PRP antibodies in the MenCCRM Group.

#### **Primary Efficacy Results:**

Percentage of subjects with titers  $\geq 1:8$ ,  $1:32$  or  $1:128$  and GMTs for rSBA-MenC antibodies (ATP cohort for antibody persistence)

Group	Timing	N	$\geq 1:8$				$\geq 1:32$			
			n	%	95% CI		n	%	95% CI	
					LL	UL			UL	LL
HibMenC	PRE	54	5	9.3	3.1	20.3	3	5.6	1.2	15.4
	PII(M6)	57	57	100	93.7	100	57	100	93.7	100
	PIII(M7)	57	57	100	93.7	100	57	100	93.7	100
	Pre booster	55	54	98.2	90.3	100	53	96.4	87.5	99.6
	PIV(M1)	43	43	100	91.8	100	43	100	91.8	100
	PIV(M18)	45	44	97.8	88.2	99.9	40	88.9	75.9	96.3
	PIV(M30)	48	39	81.3	67.4	91.1	36	75.0	60.4	86.4

	PIV(M42)	50	39	78.0	64.0	88.5	38	76.0	61.8	86.9
<b>NeisPoo</b>	PRE	116	19	16.4	10.2	24.4	12	10.3	5.5	17.4
	PII(M6)	118	118	100	96.9	100	117	99.2	95.4	100
	Pre booster	115	101	87.8	80.4	93.2	94	81.7	73.5	88.3
	PIV(M1)	96	96	100	96.2	100	95	99.0	94.3	100
	PIV(M18)	96	93	96.9	91.1	99.4	93	96.9	91.1	99.4
	PIV(M30)	101	96	95.0	88.8	98.4	94	93.1	86.2	97.2
	PIV(M42)	110	106	96.4	91.0	99.0	100	90.9	83.9	95.6
<b>HibCPoo</b>	PRE	170	24	14.1	9.3	20.3	15	8.8	5.0	14.1
	PIV(M1)	139	139	100	97.4	100	138	99.3	96.1	100
	PIV(M18)	141	137	97.2	92.9	99.2	133	94.3	89.1	97.5
	PIV(M30)	149	135	90.6	84.7	94.8	130	87.2	80.8	92.1
	PIV(M42)	160	145	90.6	85.0	94.7	138	86.3	79.9	91.2
<b>MenCCRM</b>	PRE	53	9	17.0	8.1	29.8	5	9.4	3.1	20.7
	PII(M6)	55	53	96.4	87.5	99.6	53	96.4	87.5	99.6
	PIII(M7)	56	55	98.2	90.4	100	55	98.2	90.4	100
	Pre booster	54	45	83.3	70.7	92.1	42	77.8	64.4	88.0
	PIV(M30)	45	31	68.9	53.4	81.8	25	55.6	40.0	70.4
	PIV(M42)	52	33	63.5	49.0	76.4	30	57.7	43.2	71.3
		<b>≥ 1:128</b>					<b>GMT</b>			
		<b>n</b>	<b>%</b>	<b>95% CI</b>		<b>value</b>	<b>95% CI</b>			
				<b>LL</b>	<b>UL</b>		<b>LL</b>	<b>UL</b>		
<b>HibMenC</b>	PRE	54	0	0.0	0.0	6.6	4.8	4.1	5.7	
	PII(M6)	57	55	96.5	87.9	99.6	780.0	612.4	993.5	
	PIII(M7)	57	56	98.2	90.6	100	2574.9	2054.9	3226.5	
	Pre booster	55	44	80.0	67.0	89.6	343.2	241.2	488.3	
	PIV(M1)	43	43	100	91.8	100	5223.1	3864.6	7059.2	
	PIV(M18)	45	27	60.0	44.3	74.3	221.5	137.2	357.7	
	PIV(M30)	48	27	56.3	41.2	70.5	109.1	61.9	192.3	
	PIV(M42)	50	30	60.0	45.2	73.6	98.9	56.7	172.5	
<b>NeisPoo</b>	PRE	116	6	5.2	1.9	10.9	6.3	5.1	7.7	
	PII(M6)	118	115	97.5	92.7	99.5	1329.5	1079.9	1636.7	
	Pre booster	115	67	58.3	48.7	67.4	115.2	84.6	157.0	
	PIV(M1)	96	95	99.0	94.3	100	10112.8	7547.0	13551.0	
	PIV(M18)	96	82	85.4	76.7	91.8	801.1	570.3	1125.3	
	PIV(M30)	101	80	79.2	70.0	86.6	441.7	309.4	630.6	
	PIV(M42)	110	89	80.9	72.3	87.8	409.8	297.7	564.2	
<b>HibCPoo</b>	PRE	170	6	3.5	1.3	7.5	5.8	4.9	6.7	
	PIV(M1)	139	138	99.3	96.1	100	8243.4	6573.5	10337.4	
	PIV(M18)	141	109	77.3	69.5	83.9	531.5	397.1	711.6	
	PIV(M30)	149	107	71.8	63.9	78.9	281.5	205.0	386.6	
	PIV(M42)	160	119	74.4	66.9	80.9	262.8	195.6	353.2	
<b>MenCCRM</b>	PRE	53	0	0.0	0.0	6.7	5.6	4.5	6.9	
	PII(M6)	55	52	94.5	84.9	98.9	1073.4	717.8	1605.2	
	PIII(M7)	56	54	96.4	87.7	99.6	1533.1	1097.5	2141.7	
	Pre booster	54	29	53.7	39.6	67.4	99.5	59.3	166.8	
	PIV(M30)	45	12	26.7	14.6	41.9	40.3	21.9	74.1	
	PIV(M42)	52	13	25.0	14.0	38.9	36.1	20.4	63.8	

N = number of subjects with available results

n (%) = number (percentage) of subjects with titre within the specified range

95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

PRE = Pre primary vaccination

PII(M6) = Post primary dose 2(Month 6)

PIII(M7) = Post primary dose 3(Month 7)

Pre Booster = Pre booster dose PIV(M1) = Post booster dose (Month 1) PIV(M18) = Post booster dose (Month 18) PIV(M30) = Post booster dose (Month 30) PIV(M42) = Post booster dose (Month 42)													
<b>Primary Efficacy Results:</b> Percentage of subjects with concentrations $\geq 0.3 \mu\text{g/mL}$ & $\geq 0.2 \mu\text{g/mL}$ and GMCs for anti-PSC antibodies (ATP cohort for antibody persistence)													
Group	Timing	N	$\geq 0.3 \mu\text{g/mL}$				$\geq 2 \mu\text{g/mL}$				GMC		
			n	%	95% CI		n	%	95% CI		value	95% CI	
					LL	UL			LL	UL		LL	UL
HibMenC	PRE	57	13	22.8	12.7	35.8	1	1.8	0.0	9.4	0.22	0.18	0.28
	PII(M6)	56	56	100	93.6	100	56	100	93.6	100	13.49	11.43	15.92
	PIII(M7)	52	52	100	93.2	100	52	100	93.2	100	22.38	18.71	26.76
	Pre Booster	55	52	94.5	84.9	98.9	13	23.6	13.2	37.0	1.04	0.84	1.31
	PIV(M1)	57	57	100	93.7	100	53	93.0	83.0	98.1	7.15	5.63	9.09
	PIV(M18)	56	38	67.9	54.0	79.7	1	1.8	0.0	9.6	0.50	0.39	0.64
	PIV(M30)	52	19	36.5	23.6	51.0	1	1.9	0.0	10.3	0.26	0.21	0.33
	PIV(M42)	49	17	34.7	21.7	49.6	0	0.0	0.0	7.3	0.25	0.20	0.31
NeisPoo	PRE	119	36	30.3	22.2	39.3	6	5.0	1.9	10.7	0.28	0.23	0.34
	PIII(M7)	117	117	100	96.9	100	112	95.7	90.3	98.6	10.12	8.74	11.71
	Pre Booster	120	78	65.0	55.8	73.5	5	4.2	1.4	9.5	0.45	0.38	0.53
	PIV(M1)	121	119	98.3	94.2	99.8	115	95.0	89.5	98.2	10.16	8.26	12.50
	PIV(M18)	122	100	82.0	74.0	88.3	31	25.4	18.0	34.1	1.01	0.80	1.29
	PIV(M30)	108	58	53.7	43.8	63.3	18	16.7	10.2	25.1	0.47	0.37	0.61
	PIV(M42)	107	52	48.6	38.8	58.5	14	13.1	7.3	21.0	0.40	0.32	0.51
HibCPoo	PRE	176	49	27.8	21.4	35.1	7	4.0	1.6	8.0	0.26	0.22	0.30
	PII(M6)	173	173	100	97.9	100	168	97.1	93.4	99.1	11.10	9.91	12.44
	Pre Booster	175	130	74.3	67.1	80.6	18	10.3	6.2	15.8	0.59	0.51	0.68
	PIV(M1)	178	176	98.9	96.0	99.9	168	94.4	89.9	97.3	9.08	7.73	10.67
	PIV(M18)	178	138	77.5	70.7	83.4	32	18.0	12.6	24.4	0.81	0.67	0.98
	PIV(M30)	160	77	48.1	40.2	56.2	19	11.9	7.3	17.9	0.39	0.32	0.47
	PIV(M42)	156	69	44.2	36.3	52.4	14	9.0	5.0	14.6	0.35	0.29	0.42
MenCCRM	PRE	56	12	21.4	11.6	34.4	2	3.6	0.4	12.3	0.22	0.18	0.28
	PII(M6)	52	52	100	93.2	100	51	98.1	89.7	100	13.56	10.95	16.81
	PIII(M7)	54	54	100	93.4	100	54	100	93.4	100	22.10	18.11	26.98
	Pre Booster	54	49	90.7	79.7	96.9	25	46.3	32.6	60.4	1.41	1.05	1.90
	PIV(M30)	53	19	35.8	23.1	50.2	3	5.7	1.2	15.7	0.30	0.23	0.39
	PIV(M42)	52	17	32.7	20.3	47.1	2	3.8	0.5	13.2	0.28	0.21	0.37
N = number of subjects with available results n (%) = number (percentage) of subjects with titre within the specified range 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit PRE = Pre primary vaccination PII(M6) = Post primary dose 2(Month 6) PIII(M7) = Post primary dose 3(Month 7) PRE BOOSTER = Pre booster dose PIV(M1) = Post booster dose (Month 1) PIV(M18) = Post booster dose (Month 18) PIV(M30) = Post booster dose (Month 30) PIV(M42) = Post booster dose (Month 42)													
<b>Primary Efficacy Results:</b> Percentage of subjects with concentrations $\geq 0.15 \mu\text{g/mL}$ & $\geq 1 \mu\text{g/mL}$ and GMCs for anti-PRP antibodies (ATP cohort for antibody persistence)													
Group	Timing	N	$\geq 0.15 \mu\text{g/ml}$				$\geq 1 \mu\text{g/ml}$				GMC		
			n	%	95% CI		n	%	95% CI		value	95% CI	

					LL	UL			LL	UL		LL	UL
<b>HibMenC</b>	P1I(M6)	57	56	98.2	90.6	100	44	77.2	64.2	87.3	2.987	2.069	4.313
	P1I1I(M7)	57	57	100	93.7	100	57	100	93.7	100	12.462	10.046	15.459
	Pre Booster	56	55	98.2	90.4	100	24	42.9	29.7	56.8	0.821	0.612	1.101
	P1V(M1)	57	57	100	93.7	100	57	100	93.7	100	61.534	44.907	84.318
	P1V(M18)	56	56	100	93.6	100	44	78.6	65.6	88.4	2.921	2.150	3.968
	P1V(M30)	53	53	100	93.3	100	36	67.9	53.7	80.1	1.914	1.383	2.648
	P1V(M42)	50	50	100	92.9	100	33	66.0	51.2	78.8	1.735	1.243	2.423
<b>NeisPoo</b>	P1I(M6)	121	115	95.0	89.5	98.2	74	61.2	51.9	69.9	1.713	1.300	2.258
	P1I1I(M7)	121	121	100	97.0	100	110	90.9	84.3	95.4	6.994	5.603	8.731
	Pre Booster	122	116	95.1	89.6	98.2	54	44.3	35.3	53.5	0.877	0.702	1.096
	P1V(M1)	121	121	100	97.0	100	119	98.3	94.2	99.8	70.264	54.565	90.480
	P1V(M18)	122	121	99.2	95.5	100	112	91.8	85.4	96.0	5.450	4.390	6.766
	P1V(M30)	113	112	99.1	95.2	100	98	86.7	79.1	92.4	3.524	2.813	4.415
	P1V(M42)	110	109	99.1	95.0	100	91	82.7	74.3	89.3	2.986	2.395	3.722
<b>HibCPoo</b>	P1I(M6)	178	171	96.1	92.1	98.4	118	66.3	58.8	73.2	2.047	1.638	2.558
	P1I1I(M7)	178	178	100	97.9	100	167	93.8	89.2	96.9	8.415	7.104	9.968
	Pre Booster	178	171	96.1	92.1	98.4	78	43.8	36.4	51.4	0.859	0.720	1.026
	P1V(M1)	178	178	100	97.9	100	176	98.9	96.0	99.9	67.342	55.257	82.069
	P1V(M18)	178	177	99.4	96.9	100	156	87.6	81.9	92.1	4.479	3.740	5.364
	P1V(M30)	166	165	99.4	96.7	100	134	80.7	73.9	86.4	2.900	2.402	3.501
	P1V(M42)	160	159	99.4	96.6	100	124	77.5	70.2	83.7	2.520	2.092	3.036
<b>MenCCRM</b>	P1I(M6)	56	46	82.1	69.6	91.1	17	30.4	18.8	44.1	0.618	0.386	0.989
	P1I1I(M7)	56	55	98.2	90.4	100	46	82.1	69.6	91.1	3.521	2.430	5.102
	Pre Booster	55	47	85.5	73.3	93.5	19	34.5	22.2	48.6	0.551	0.398	0.763
	P1V(M1)	56	56	100	93.6	100	56	100	93.6	100	49.427	35.962	67.933
	P1V(M18)	3	3	100	29.2	100	3	100	29.2	100	2.547	0.390	16.651
	P1V(M30)	53	53	100	93.3	100	40	75.5	61.7	86.2	2.224	1.578	3.133
	P1V(M42)	51	51	100	93.0	100	34	66.7	52.1	79.2	2.005	1.365	2.946

N = number of subjects with available results  
n (%) = number (percentage) of subjects with concentration within the specified range  
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit  
P1I(M6) = Post primary dose 2(Month 6)  
P1I1I(M7) = Post primary dose 3(Month 7)  
PRE BOOSTER = Pre booster dose  
P1V(M1) = Post booster dose (Month 1)  
P1V(M18) = Post booster dose (Month 18)  
P1V(M30) = Post booster dose (Month 30)  
P1V(M42) = Post booster dose (Month 42)

**Secondary Outcome Variable (s):** Not applicable.

**Safety results:** Number (%) of subjects with serious adverse events (SAEs), determined by the investigator to have a causal relationship to the study vaccination and occurring from the last study contact of the booster study until the end of the first long term persistence study (Total cohort Year 1)

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

All SAEs	HibMenC Group N = 58	NeisPoo Group N = 123	HibCPoo Group N = 181	MenCCRM Group N = 3
Subjects with any SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	HibMenC Group N = 58	NeisPoo Group N = 123	HibCPoo Group N = 181	MenCCRM Group N = 3
Subjects with Fatal SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

**Safety results:** Number (%) of subjects with serious adverse events (SAEs), determined by the investigator to have a causal relationship to the study vaccination and occurring from the last study contact of the booster study until the end of the second long-term persistence study (Total cohort Year 2)

<b>Serious adverse event, n (%) [n considered by the investigator to be related to study medication]</b>				
<b>All SAEs</b>	<b>HibMenC Group N = 54</b>	<b>NeisPoo Group N = 119</b>	<b>HibCPoo Group N = 173</b>	<b>MenCCRM Group N = 57</b>
Subjects with any SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
<b>Fatal SAEs</b>	<b>HibMenC Group N = 54</b>	<b>NeisPoo Group N = 119</b>	<b>HibCPoo Group N = 173</b>	<b>MenCCRM Group N = 57</b>
Subjects with Fatal SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
<b>Safety results:</b> Number (%) of subjects with serious adverse events (SAEs), determined by the investigator to have a causal relationship to the study vaccination and occurring from the last study contact of the booster study until the end of the third long-term persistence study (Total cohort Year 3)				
<b>Serious adverse event, n (%) [n considered by the investigator to be related to study medication]</b>				
<b>All SAEs</b>	<b>HibMenC Group N = 51</b>	<b>NeisPoo Group N = 113</b>	<b>HibCPoo Group N = 164</b>	<b>MenCCRM Group N = 56</b>
Subjects with any SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
<b>Fatal SAEs</b>	<b>HibMenC Group N = 51</b>	<b>NeisPoo Group N = 113</b>	<b>HibCPoo Group N = 164</b>	<b>MenCCRM Group N = 56</b>
Subjects with Fatal SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

**Conclusion:**

For study 106672, please refer to the publication below.

Thirty months after the booster vaccination course, overall 93.9% (HibMenC Group: 88.0%, NeisPoo Group: 96.5%) of all subjects boosted with Hib-MenC and 79.2% of the subjects in the MenCCRM Group had rSBA-MenC titers  $\geq 1:8$ . At the same time point, overall 99.4% (HibMenC Group: 100%, NeisPoo Group: 99.1%) of all subjects boosted with Hib-MenC and 100% of the subjects in the MenCCRM Group had anti-PRP antibody concentrations  $\geq 0.15 \mu\text{g/mL}$ .

Forty-two months after the booster vaccination course, overall 90.6% (HibMenC Group: 78.0%, NeisPoo Group: 96.4%) of all subjects boosted with Hib-MenC and 63.5% of the subjects in the MenCCRM Group had rSBA-MenC titers  $\geq 1:8$ . At the same time point, overall 99.4% (HibMenC Group: 100%, NeisPoo Group: 99.1%) of all subjects boosted with Hib-MenC and 100% of the subjects in the MenCCRM Group had anti-PRP antibody concentrations  $\geq 0.15 \mu\text{g/mL}$ .

No SAE related to study vaccination was reported from the last study contact of the booster study until 42 months after the booster vaccination.

**Publications:** Tejedor JC et al. (2008) Immunogenicity and Reactogenicity of a Booster Dose of a Novel Combined Haemophilus influenzae Type b-Neisseria meningitidis Serogroup C-Tetanus Toxoid Conjugate Vaccine Given to Toddlers of 13–14 Months of Age With Antibody Persistence Up to 31 Months of Age. *Pediatr Infect Dis J.* 27(7): 579–588.

Date updated: 28 September 2009