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<b>Study No.:</b> 106445 (Hib-MenC-TT-016) & 106446 (Hib-MenC-TT-017 EXT:016 Y1)
<p><b>Title:</b> A phase III, open, randomized, controlled, multi-centre study to demonstrate the non-inferiority of the meningococcal serogroup C and the <i>Haemophilus influenzae</i> type b immune response of GlaxoSmithKline (GSK) Biologicals' conjugate Hib-MenC vaccine co-administered with GSK Biologicals' measles-mumps-rubella vaccine, Priorix™, versus MenC-CRM<sub>197</sub> conjugate vaccine co-administered with GSK Biologicals' Hib vaccine, Hiberix™, and Priorix™ in 12- to 18-month-old toddlers primed in infancy with a Hib vaccine but not with a meningococcal serogroup C vaccine; and to evaluate the long-term antibody persistence up to 5 years after the administration of the Hib-MenC vaccine.</p> <p>Menitorix™ (Hib-MenC): GlaxoSmithKline (GSK) Biologicals' <i>Haemophilus influenzae</i> type b-meningococcal serogroup C tetanus toxoid conjugate vaccine.</p> <p>Priorix™ (MMR): GSK Biologicals' combined measles-mumps-rubella vaccine.</p> <p>Hiberix™ (Hib): GSK Biologicals' <i>Haemophilus influenzae</i> type b vaccine.</p> <p>Meningitec™ (MCC): Wyeth's meningococcal serogroup C CRM<sub>197</sub> conjugated vaccine.</p>
<p><b>Rationale:</b> The aim of the study was to demonstrate the non-inferiority and to evaluate the Hib and MenC long-term antibody persistence elicited by Hib-MenC vaccine versus MCC vaccine co-administered with Hib vaccine, when co-administered with MMR vaccine in 12- to 18-month-old toddlers primed in infancy with a Hib vaccine but not with a serogroup C meningococcal vaccine.</p> <p>Note: This study has 2 phases: the vaccination phase and the long-term persistence phase with assessments of Hib and MenC long-term antibody persistence at 1, 2, 3, 4 and 5 years after vaccination.</p> <p>This CTRS presents the results for the vaccination phase and the Year 1 (12 months post vaccination) of the long-term persistence phase. The summary will be updated as soon as the data become available.</p>
<b>Phase:</b> III
<p><b>Study Period:</b></p> <p>Hib-MenC-TT-016: 19 June 2006 to 06 November 2007</p> <p>Hib-MenC-TT-017: 04 July 2007 to 14 October 2008 (EXT Year 1)</p>
<b>Study Design:</b> Open, randomized [3:1], controlled, multi-centre study with 2 parallel groups.
<b>Centers:</b> 7 study centers in Australia.
<b>Indication:</b> Immunization against meningococcal serogroup C & <i>Haemophilus influenzae</i> type b diseases.
<p><b>Treatment:</b> The study groups are as follows:</p> <ul style="list-style-type: none"> <li>• Hib-MenC Group received a single dose of Hib-MenC vaccine co-administered with MMR vaccine.</li> <li>• MCC+ Hib Group received a single dose of MCC vaccine co-administered with Hib and MMR vaccines.</li> </ul> <p>The Hib-MenC and MCC vaccines were administered intramuscularly in the left deltoid region, the Hib vaccine was administered intramuscularly in the left thigh region and the MMR vaccine was administered subcutaneously in the right upper arm.</p>
<p><b>Objectives:</b></p> <p><i>One month after vaccination:</i></p> <p>To demonstrate the non-inferiority of the meningococcal serogroup C and Hib responses induced by Hib-MenC vaccine, compared to separately administered MCC and Hib (with MMR co-administered in each group), when given as a single dose to toddlers 12-18 months of age primed with routine infant vaccines including Hib, but no MenC vaccine, in terms of:</p> <ul style="list-style-type: none"> <li>• Percentage of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titer <math>\geq</math> 1:8.</li> <li>• Percentage of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration <math>\geq</math> 0.15 <math>\mu</math>g/mL.</li> </ul> <p>Criterion for achieving the co-primary objectives: One month after vaccination, the lower limit of the standardized asymptotic 95% confidence interval on the difference between the study vaccine group and (minus) the control group was above -10%.</p>
<p><b>Primary Outcome/Efficacy Variable:</b></p> <p>One month after vaccination, in all evaluable subjects:</p> <ul style="list-style-type: none"> <li>• rSBA-MenC titers <math>\geq</math> 1:8</li> <li>• Anti-PRP concentration <math>\geq</math> 0.15 <math>\mu</math>g/mL.</li> </ul>
<p><b>Secondary Outcome/Efficacy Variable(s):</b></p> <p><i>Immunogenicity:</i></p>

Prior to vaccination, in all evaluable subjects:

- rSBA-MenC titers  $\geq 1:8$ .
- Anti-PRP antibody concentration  $\geq 0.15 \mu\text{g/mL}$ .

Prior to and one month after vaccination, in all evaluable subjects:

- rSBA-MenC titer  $\geq 1:128$  and titers.
- Anti-PRP antibody concentration  $\geq 1.0 \mu\text{g/mL}$  and concentrations.
- Anti-polysaccharide C (anti-PSC) concentration  $\geq 0.30 \mu\text{g/mL}$ ,  $\geq 2.0 \mu\text{g/mL}$  and concentrations.

1, 2, 3, 4, and 5 years after vaccination (for evaluation of the Hib and MenC antibody persistence), in all evaluable subjects<sup>†</sup>:

- rSBA-MenC titers  $\geq 1:8$ ,  $\geq 1:128$ , and titers.
- Anti-PRP antibody concentration  $\geq 0.15 \mu\text{g/mL}$ ,  $\geq 1.0 \mu\text{g/mL}$  and concentrations.
- Anti-PSC antibody concentrations  $\geq 0.30 \mu\text{g/mL}$ ,  $\geq 2.0 \mu\text{g/mL}$ , and concentrations

**Safety:**

- Occurrence of solicited local (pain, redness and swelling) and general (irritability / fussiness, fever, drowsiness and loss of appetite) symptoms within 4 days (Day 0-3) after vaccination.
- Occurrence of unsolicited symptoms within 31 days (Day 0–30) after vaccination.
- Occurrence of serious adverse events (SAEs) throughout the entire study period.\* †

\*Note: At each visit of the long-term persistence phase (i.e. at 1 year up to 5 years after vaccination) it will be asked retrospectively to the subject's parents/guardians if any SAE, as defined hereafter, has occurred since the last visit of the previous year. Only those SAEs that are determined by the investigator to have a causal relationship to the vaccination will be described individually.

†The summary will be updated when data become available for Year 2, 3, 4 and 5.

**Statistical Methods:** The analyses were performed on the Total Vaccinated Cohort, the According-to-Protocol (ATP) cohort for immunogenicity, the Total Enrolled Cohort Year 1 and the ATP cohort for persistence for Y1.

- The Total Vaccinated Cohort included all vaccinated subjects for whom data were available for the vaccination phase.
- The ATP cohort for immunogenicity included all evaluable subjects (i.e. those meeting all eligibility criteria, complying with the procedures defined in the protocol, and with no elimination criteria during the study) for whom assay results were available for antibodies against at least one study vaccine antigen component for the blood sample taken one month after the vaccinations.
- Total Enrolled Cohort Year 1 included all vaccinated subjects in the vaccination phase (study Hib-MenC-TT-016) who came back for the Year 1 follow-up.
- ATP cohort for persistence for Year 1 included all evaluable subjects: who received the vaccines during the vaccination phase; who did not receive a previous dose of Hib or meningococcal serogroup C vaccines other than the study vaccines during the vaccination phase; who had available assay results for at least one tested antigen at the year 1 timepoint.

**Analysis of Immunogenicity:**

The analysis of immunogenicity was performed on the ATP cohort for immunogenicity and the ATP cohort for persistence for Year 1.

*Inferential analysis*

The asymptotic standardized 95% confidence interval (CI) for the difference between the Hib-MenC Group and (minus) the MCC + Hib Group in the percentage of subjects with rSBA-MenC titer  $\geq 1:8$  and with anti-PRP antibody concentrations  $\geq 0.15 \mu\text{g/mL}$ , one month after vaccination, was computed. The co-primary objectives were met if the lower limits of these 95% CI were both above  $-10\%$ .

*Descriptive analysis*

For each treatment group, prior to and one month after the vaccination, for each antibody assessed at the corresponding time point, percentages of subjects with titers or concentrations above proposed cut-offs with exact 95% CIs were tabulated along with the geometric mean antibody concentrations or titers (GMCs or GMTs) with 95% CIs. Antibody concentrations or titres below the assay cut-off were given an arbitrary value of half the cut-off for the purpose of GMTs or GMCs calculation.

**Analysis of Safety:**

The analysis of safety was performed on the Total Vaccinated Cohort and the Total Enrolled Cohort Year 1.

The percentage of subjects with each individual solicited local (any grade, grade 3) and general (any grade, grade 3, related) symptom during the 4-day follow-up period (Day 0–3) after vaccination and its exact 95% CI was tabulated. The percentage of subjects with unsolicited adverse events (AEs) within 31 days post-vaccination (Day 0-30) and its exact 95% CI was tabulated by group according to the Medical Dictionary of Regulatory Activities (MedDRA) preferred terms.

The occurrence of SAEs during the entire study period was tabulated according MedDRA preferred terms.										
<b>Study Population:</b> Healthy male or female subjects between, and including, 12 and 18 months of age at the time of vaccination, free of obvious health problems, who had previously completed routine childhood vaccinations including completed primary vaccination with 2 doses of Hib-outer membrane protein (Hib-OMP) containing vaccine or 3 doses of diphtheria-tetanus-acellular pertussis, Hib-tetanus toxoid (TT) (DTPa/Hib) containing vaccine at least 6 months before the study start were enrolled. Written informed consent was obtained from the parent or guardian of the subject before study start.										
<b>Number of subjects</b>			<b>Hib-MenC Group</b>			<b>MCC + Hib Group</b>				
Planned, N			324			109				
Randomized, N (Total Vaccinated Cohort)			324			109				
Completed, n (%)			320 (98.8)			108 (99.1)				
Total Number Subjects Withdrawn, n (%)			4 (1.2)			1 (0.9)				
Withdrawn due to Adverse Events, n (%)			0 (0.0)			0 (0.0)				
Withdrawn due to Lack of Efficacy, n (%)			Not applicable			Not applicable				
Withdrawn for other reasons, n (%)			4 (1.2)			1 (0.9)				
<b>Demographics</b>			<b>Hib-MenC Group</b>			<b>MCC + Hib Group</b>				
N (Total Vaccinated Cohort)			324			109				
Females: Males			150:174			42:67				
Mean Age, months (SD)			12.5 (0.94)			12.5 (0.75)				
White - Caucasian / European heritage, n (%)			278 (85.8)			101 (92.7)				
<b>Number of subjects</b>			<b>HibMenC Group</b>			<b>MCC + Hib Group</b>				
Planned, N			324			109				
Entered, N (Total Enrolled Cohort Year 1)			295			100				
Entered, N (ATP cohort for Persistence Year 1)			264			93				
Completed, n (%)			295(100)			109(100)				
Total Number Subjects Withdrawn, n (%)			NA			NA				
<b>Demographics</b>			<b>HibMenC Group</b>			<b>MCC + Hib Group</b>				
N (Total Enrolled Cohort Year 1)			295			100				
Females:Males			137:158			38:62				
Mean Age, months (SD)			24.6 (1.11)			24.6 (1.08)				
White - Caucasian / European heritage, n (%)			254 (86.1)			93 (93.0)				
<b>Primary Efficacy Results:</b> Difference between the Hib-MenC Group and (minus) the MCC + Hib Group in terms of percentages of subjects with rSBA-MenC titer $\geq 1:8$ , one month after the administration of the vaccine dose (ATP Cohort for Immunogenicity)										
Group	N	%	Group	N	%	Difference in percentage of subjects with rSBA-MenC $\geq 1:8$ (Hib-MenC Group minus MCC + Hib Group)				
						Difference		%	95% CI	
						LL	UL			
<b>Hib-MenC</b>	281	99.6	<b>MCC + Hib</b>	98	100	Hib-MenC – MCC+ Hib	-0.36	-1.99	3.43	
N = number of subjects with available results % = percentage of subjects with rSBA-MenC titer $\geq 1:8$ 95% CI = 95% standardized asymptotic confidence interval; LL = Lower Limit, UL = Upper Limit Primary objective met since the LL of the 95% CI is above -10%.										
<b>Primary Efficacy Results:</b> Difference between the Hib-MenC Group and (minus) the MCC + Hib Group in terms of percentages of subjects with anti-PRP antibody concentrations $\geq 0.15\mu\text{g/mL}$ , one month after the administration of the vaccine dose (ATP Cohort for Immunogenicity)										
Group	N	%	Group	N	%	Difference in percentage of subjects with anti-PRP antibody concentrations $\geq 0.15 \mu\text{g/mL}$ (Hib-MenC Group minus MCC + Hib Group)				
						Difference		%	95% CI	
						LL	UL			
<b>Hib-MenC</b>	292	100	<b>MCC + Hib</b>	100	100	Hib-MenC – MCC + Hib	0.00	-1.30	3.71	
N = number of subjects with available results % = percentage of subjects with anti-PRP antibody concentration $\geq 0.15 \mu\text{g/mL}$										

95% CI = 95% standardized asymptotic confidence interval; LL = Lower Limit, UL = Upper Limit Primary objective met since the LL of the 95% CI is above -10%.														
<b>Primary Efficacy Results:</b> Percentage of subjects with $\geq 1:8$ or $1:128$ and GMTs for rSBA-MenC antibodies, pre-vaccination and one month after the administration of the vaccine dose (ATP Cohort for Immunogenicity)														
Antibody	Group	Timing	N	$\geq 1:8^*$				$\geq 1:128$				GMT		
				n	%	95% CI		n	%	95% CI		Value	95% CI	
						LL	UL			LL	UL		LL	UL
rSBA-MenC	Hib-MenC	PRE	255	37	14.5	10.4	19.4	15	5.9	3.3	9.5	6.3	5.5	7.3
		PI(MI)	281	280	99.6	98.0	100	247	87.9	83.5	91.5	482.8	420.7	554.2
	MCC + Hib	PRE	83	7	8.4	3.5	16.6	3	3.6	0.8	10.2	5.5	4.3	7.2
		PI(MI)	98	98	100	96.3	100	89	90.8	83.3	95.7	621.0	480.3	802.9
N = number of subjects with available results n (%) = number (percentage) of subjects with titer within the specified range 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit Pre = pre-vaccination blood sample PI(MI) = post-vaccination blood sample at Month 1 * Primary efficacy result														
<b>Primary Efficacy Results:</b> Percentage of subjects with $\geq 1:8$ or $1:128$ and GMTs for rSBA-MenC antibodies at Year 1 (ATP cohort for Persistence Year 1)														
Antibody	Group	Timing	N	$\geq 1:8^*$				$\geq 1:128$				GMT		
				n	%	95% CI		n	%	95% CI		Value	95% CI	
						LL	UL			LL	UL		LL	UL
rSBA-MenC	Hib-MenC	PRE †	230	31	13.5	9.3	18.6	12	5.2	2.7	8.9	6.1	5.2	7.0
		PI(MI) †	252	251	99.6	97.8	100	220	87.3	82.5	91.1	482.8	416.5	559.6
		PI(M12) †	249	216	86.7	81.9	90.7	117	47.0	40.7	53.4	91.7	75.6	111.3
	MCC + Hib	PRE †	77	5	6.5	2.1	14.5	1	1.3	0.0	7.0	4.9	4.1	5.8
		PI(MI) †	90	90	100	96.0	100	82	91.1	83.2	96.1	566.3	437.9	732.4
		PI(M12) †	89	68	76.4	66.2	84.8	37	41.6	31.2	52.5	63.8	43.3	94.1
N = number of subjects with available results n (%) = number (percentage) of subjects with titer within the specified range 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit Pre = pre-vaccination blood sample PI(MI) = post-vaccination blood sample at Month 1 PI(M12) = post-vaccination blood sample at Month 12 *Primary efficacy result † Analyses of persistence were done on the ATP Cohort for Persistence at a particular timepoint, which include all vaccinated subjects in the vaccination phase (study Hib-MenC-TT-016) who came back for the year x follow-up														
<b>Primary Efficacy Results:</b> Percentage of subjects with antibody concentrations $\geq 0.15 \mu\text{g/mL}$ or $1.0 \mu\text{g/mL}$ and GMCs for anti-PRP antibodies, pre-vaccination and one after the administration of the vaccine dose (ATP Cohort for Immunogenicity)														
Antibody	Group	Timing	N	$\geq 0.15 \mu\text{g/mL}^*$				$\geq 1.0 \mu\text{g/mL}$				GMC ( $\mu\text{g/mL}$ )		
				n	%	95% CI		n	%	95% CI		Value	95% CI	
						LL	UL			LL	UL		LL	UL
Anti-PRP	Hib-MenC	PRE	285	219	76.8	71.5	81.6	77	27.0	21.9	32.6	0.438	0.374	0.512
		PI(MI)	292	292	100	98.7	100	286	97.9	95.6	99.2	46.652	38.929	55.907
	MCC + Hib	PRE	98	82	83.7	74.8	90.4	22	22.4	14.6	32.0	0.472	0.364	0.611
		PI(MI)	100	100	100	96.4	100	100	100	96.4	100	73.976	57.624	94.968
N = number of subjects with available results n (%) = number (percentage) of subjects with antibody concentration within the specified range 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit Pre = pre-vaccination blood sample PI(MI) = post-vaccination blood sample at Month 1 * Primary efficacy result														
<b>Primary Efficacy Results:</b> Percentage of subjects with antibody concentrations $\geq 0.15 \mu\text{g/mL}$ or $1.0 \mu\text{g/mL}$ and GMCs for anti-PRP antibodies at Year 1 (ATP cohort for Persistence Year 1)														
Antibody	Group	Timing	N	$\geq 0.15 \mu\text{g/mL}^*$				$\geq 1.0 \mu\text{g/mL}$				GMC ( $\mu\text{g/mL}$ )		

Anti-PRP				n	%	95% CI		n	%	95% CI		Value	95% CI	
						LL	UL			LL	UL		LL	UL
Hib-MenC	PRE †	256	196	76.6	70.9	81.6	71	27.7	22.3	33.7	0.440	0.372	0.520	
	PI(MI) †	261	261	100	98.6	100	255	97.7	95.1	99.2	46.955	38.683	56.995	
	PI(M12) †	255	252	98.8	96.6	99.8	209	82.0	76.7	86.5	3.550	2.988	4.218	
MCC + Hib	PRE †	91	74	81.3	71.8	88.7	20	22.0	14.0	31.9	0.444	0.338	0.582	
	PI(MI) †	92	92	100	96.1	100	92	100	96.1	100	72.645	55.595	94.924	
	PI(M12) †	91	91	100	96.0	100	80	87.9	79.4	93.8	4.802	3.708	6.218	

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  
Pre = pre-vaccination blood sample  
PI(MI) = post-vaccination blood sample at Month 1  
PI(M12) = post-vaccination blood sample at Month 12  
\* Primary efficacy result

† Analyses of persistence were done on the ATP Cohort for Persistence at a particular timepoint, which include all vaccinated subjects in the vaccination phase (study Hib-MenC-TT-016) who came back for the year x follow-up

**Secondary Outcome Variable(s):** Percentage of subjects with antibody concentrations  $\geq 0.3 \mu\text{g/mL}$  or  $2 \mu\text{g/mL}$  and GMCs for anti-PSC antibodies, pre-vaccination and one month after the administration of the vaccine dose (ATP Cohort for Immunogenicity)

Antibody	Group	Timing	N	$\geq 0.3 \mu\text{g/mL}$				$\geq 2. \mu\text{g/mL}$				GMC ( $\mu\text{g/mL}$ )		
				n	%	95% CI		n	%	95% CI		Value	95% CI	
						LL	UL			LL	UL		LL	UL
Anti-PSC	Hib-MenC	PRE	283	2	0.7	0.1	2.5	0	0.0	0.0	1.3	0.15	0.15	0.15
		PI(MI)	290	290	100	98.7	100	289	99.7	98.1	100	18.69	17.10	20.42
	MCC + Hib	PRE	96	1	1.0	0.0	5.7	0	0.0	0.0	3.8	0.15	0.15	0.16
		PI(MI)	100	100	100	96.4	100	96	96.0	90.1	98.9	7.95	6.95	9.08

N = number of subjects with available results  
n (%) = number (percentage) of subjects with antibody concentration within the specified range  
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit  
Pre = pre-vaccination blood sample  
PI(MI) = post-vaccination blood sample at Month 1

**Secondary Outcome Variable(s):** Percentage of subjects with antibody concentrations  $\geq 0.3 \mu\text{g/mL}$  or  $2 \mu\text{g/mL}$  and GMCs for anti-PSC antibodies at Year 1 (ATP cohort for Persistence Year 1)

Antibody	Group	Timing	N	$\geq 0.3 \mu\text{g/mL}$				$\geq 2. \mu\text{g/mL}$				GMC ( $\mu\text{g/mL}$ )		
				n	%	95% CI		n	%	95% CI		Value	95% CI	
						LL	UL			LL	UL		LL	UL
Anti-PSC	Hib-MenC	PRE †	254	2	0.8	0.1	2.8	0	0.0	0.0	1.4	0.15	0.15	0.15
		PI(MI) †	260	260	100	98.6	100	259	99.6	97.9	100	18.95	17.27	20.79
		PI(M12) †	250	95	38.0	32.0	44.3	6	2.4	0.9	5.2	0.27	0.24	0.30
	MCC + Hib	PRE †	89	0	0.0	0.0	4.1	0	0.0	0.0	4.1	0.15	0.15	0.15
		PI(MI) †	92	92	100	96.1	100	88	95.7	89.2	98.8	7.89	6.84	9.10
		PI(M12) †	91	33	36.3	26.4	47.0	0	0.0	0.0	4.0	0.25	0.21	0.29

N = number of subjects with available results  
n (%) = number (percentage) of subjects with antibody concentration within the specified range  
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit  
Pre = pre-vaccination blood sample  
PI(MI) = post-vaccination blood sample at Month 1  
PI(M12) = post-vaccination blood sample at Month 12

† Analyses of persistence were done on the ATP Cohort for Persistence at a particular timepoint, which include all vaccinated subjects in the vaccination phase (study Hib-MenC-TT-016) who came back for the year x follow-up

**Secondary Outcome Variable(s):** Incidence of solicited local symptoms reported during the 4-day (Days 0-3) post-vaccination period (Total Vaccinated Cohort)

Symptom	Intensity	Hib-MenC Group				MCC + Hib Group			
		N	n	%	95% CI	N	n	%	95% CI

					LL	UL				LL	UL
<b>Pain</b>	Any	317	78	24.6	20.0	29.7	109	31	28.4	20.2	37.9
	Grade 3	317	0	0.0	0.0	1.2	109	0	0.0	0.0	3.3
<b>Redness</b>	Any	317	129	40.7	35.2	46.3	109	56	51.4	41.6	61.1
	>30.0 mm	317	2	0.6	0.1	2.3	109	3	2.8	0.6	7.8
<b>Swelling</b>	Any	317	64	20.2	15.9	25.0	109	25	22.9	15.4	32.0
	>30.0 mm	317	1	0.3	0.0	1.7	109	2	1.8	0.2	6.5

N = number of subjects with the documented dose  
n (%) = number (percentage) of subjects for whom the symptom was reported at least once  
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit  
Any = occurrence of any local symptom regardless of their intensity grade  
Grade 3 Pain = Cried when limb was moved/spontaneously painful

**Secondary Outcome Variable(s):** Incidence of solicited general symptoms reported during the 4-day (Days 0-3) post-vaccination period (Total Vaccinated Cohort)

Symptom	Intensity/ Relationship	Hib-MenC Group					MCC + Hib Group				
		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL
<b>Drowsiness</b>	Any	320	102	31.9	26.8	37.3	108	40	37.0	27.9	46.9
	Grade 3	320	4	1.3	0.3	3.2	108	3	2.8	0.6	7.9
	Related	320	88	27.5	22.7	32.7	108	35	32.4	23.7	42.1
<b>Fever (Rectally)</b>	≥38 °C	320	76	23.8	19.2	28.8	108	30	27.8	19.6	37.2
	>40.0 °C	320	8	2.5	1.1	4.9	108	4	3.7	1.0	9.2
	Related	320	60	18.8	14.6	23.5	108	28	25.9	18.0	35.2
<b>Irritability</b>	Any	320	154	48.1	42.5	53.8	108	69	63.9	54.1	72.9
	Grade 3	320	16	5.0	2.9	8.0	108	3	2.8	0.6	7.9
	Related	320	132	41.3	35.8	46.9	108	60	55.6	45.7	65.1
<b>Loss of appetite</b>	Any	320	102	31.9	26.8	37.3	108	40	37.0	27.9	46.9
	Grade 3	320	4	1.3	0.3	3.2	108	0	0.0	0.0	3.4
	Related	320	82	25.6	20.9	30.8	108	35	32.4	23.7	42.1

N = number of subjects with the documented dose  
n (%) = number (percentage) of subjects for whom the symptom was reported at least once  
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit  
Any = occurrence of any general symptom regardless of their intensity grade or relationship to vaccination.  
Grade 3 Drowsiness = drowsiness that prevented normal activity  
Grade 3 Irritability = crying that could be comforted/ prevented normal activity  
Grade 3 Loss of appetite = did not eat at all  
Related = general symptom considered by the investigator to be causally related to the study vaccination

**Safety results:** Number (%) of subjects with unsolicited adverse events (Total Vaccinated Cohort)

Most frequent adverse events—On-Therapy (occurring within Day 0-30 following vaccination)	Hib-MenC Group N = 324	MCC + Hib Group N = 109
Subjects with any AE(s), n (%)	217 (67.0)	81 (74.3)
Upper respiratory tract infection	54 (16.7)	13 (11.9)
Teething	40 (12.3)	15 (13.8)
Pyrexia	37 (11.4)	13 (11.9)
Rash	24 (7.4)	17 (15.6)
Diarrhea	25 (7.7)	8 (7.3)
Vomiting	22 (6.8)	9 (8.3)
Otitis media	12 (3.7)	5 (4.6)
Rhinorrhoea	17 (5.2)	-
Gastroenteritis	16 (4.9)	-
Cough	13 (4.0)	-
Injection site reaction	-	10 (9.2)
Dermatitis diaper	-	9 (8.3)
Irritability	-	9 (8.3)

- : Adverse event absent or not meeting the selected rule(s)

Detail of rule: $\geq 30$ patients per treatment group and $\leq 3$ groups, display 10 more frequent primary preferred terms		
<b>Safety results:</b> Number (%) of subjects with serious adverse events (Total Vaccinated Cohort)		
<b>Serious adverse event, n (%) [n considered by the investigator to be related to study medication]</b>		
<b>All SAEs</b>	<b>Hib-MenC Group N = 324</b>	<b>MCC + Hib Group N = 109</b>
Subjects with any SAE(s), n (%) [n related]	4 (1.2) [0]	2 (1.8) [1]
Asthma	0 (0.0) [0]	1 (0.9) [0]
Breath holding	1 (0.3) [0]	0 (0.0) [0]
Convulsion	1 (0.3) [0]	0 (0.0) [0]
Croup infectious	1 (0.3) [0]	0 (0.0) [0]
Gastroenteritis	1 (0.3) [0]	0 (0.0) [0]
Pneumonia	0 (0.0) [0]	1 (0.9) [0]
Pyrexia	0 (0.0) [0]	1 (0.9) [1]
Rash	0 (0.0) [0]	1 (0.9) [1]
Traumatic brain injury	1 (0.3) [0]	0 (0.0) [0]
<b>Fatal SAEs</b>	<b>Hib-MenC Group N = 324</b>	<b>MCC + Hib Group N = 109</b>
Subjects with fatal SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]
<b>Safety results:</b> Number (%) of subjects with serious adverse events determined by the investigator to have a causal relationship to the study vaccination and occurring from the last study contact of the primary study until Year 1 of the long-term persistence study (Total Enrolled Cohort Year 1)		
<b>Serious adverse event, n (%) [n considered by the investigator to be related to study medication]</b>		
<b>All SAEs</b>	<b>Hib-MenC Group N = 295</b>	<b>MCC + Hib Group N = 100</b>
Subjects with any SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]
<b>Fatal SAEs</b>	<b>Hib-MenC Group N = 295</b>	<b>MCC + Hib Group N = 100</b>
Subjects with fatal SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]

**Conclusion:** One month after the administration of the vaccine dose, 99.6% and 100% of the subjects in Hib-MenC Group and MCC + Hib Group, respectively, had rSBA-MenC titer  $\geq 1:8$ . At the same time point, all subjects in both groups had anti-PRP antibody concentrations  $\geq 0.15 \mu\text{g/mL}$ . During the 31-day post-vaccination period, at least one unsolicited symptom was reported for 217 (67.0%) and 81 (74.3%) subjects in Hib-MenC and MCC + Hib groups, respectively. During the active phase of the study, SAEs were reported for 4 (1.2%) and 2 (1.8%) subjects in Hib-MenC and MCC + Hib groups, respectively; 2 SAEs reported for 1 subject in the MCC + Hib Group were assessed by the investigator as related to the study vaccination. No fatal SAEs were reported during the vaccination phase of the study. Twelve months post vaccination 86.7% and 76.4% of the subjects in Hib-MenC Group and MCC + Hib Group, respectively, had rSBA-MenC titer  $\geq 1:8$  and 98.8% and 100% of the subjects in Hib-MenC Group and MCC + Hib Group, respectively had anti-PRP antibody concentrations  $\geq 0.15 \mu\text{g/mL}$ . No SAE assessed by the investigators as related to vaccination was reported from the last study contact of the primary study until Year 1 of the long-term persistence study.

**Publications:** None.

Date of update: 22 Sep 09