

The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

<p>Study No.: 109664 (Hib-MenC-TT-027 EXT:013 M12),109666 (Hib-MenC-TT-028 EXT:013 M24)</p>
<p>Title: Assessment of long-term antibody persistence after a booster dose of GSK Biologicals' Hib & meningococcal serogroup C vaccine (Menitorix™) 471266 given at 12-15 months of age to subjects primed with 3 doses of Menitorix™ at 2, 3, 4 months of age. <i>Menitorix™</i> (Hib-MenC): GlaxoSmithKline (GSK) Biologicals' combined <i>Haemophilus influenzae</i> type b and <i>Neisseria meningitidis</i> serogroup C tetanus toxoid conjugate vaccine.</p>
<p>Rationale: The aim of this study was to evaluate the persistence of the immune response to the Hib-MenC vaccine at 2, 3 and 5 years of age in subjects who were primed in infancy at 2, 3 and 4 months of age with either Hib-MenC co-administered with <i>Infanrix</i>-IPV or with <i>Meningitec</i> co-administered with <i>Pediacel</i> in study Hib-MenC-TT-012 (103974) and who received a booster dose of Hib-MenC vaccine co-administered with <i>Priorix</i>, at 12-15 months of age in study Hib-MenC-TT-013 BST:012 (104056). As per UK national vaccination schedule, children enrolled in the UK received a DTPa-IPV booster at 3 years of age; this study also assessed the persistence of pertussis antibodies prior to the DTPa-IPV booster vaccination. Note: Visit 1 corresponds to study 109664, extension Month 12 (age 24-31 months), Visit 2 corresponds to study 109666 extension Month 24 (aged 40-43 months) and Visit 3 corresponds to study 109668 extension Month 48 (age 60-64 months). Data pertaining to Year 1 (Visit 1, extension Month 12) and Year 2 (Visit 2, extension Month 24) are presented in this CTRS; the summary will be updated when Year 4 (Visit 3, extension Month 48) data become available. For results on the primary vaccination and booster studies, please refer to 103974 and 104056 CTRS. <i>Priorix™</i> (MMR): GSK Biologicals' measles-mumps-rubella vaccine. <i>Infanrix™</i> -IPV (DTPa-IPV): GSK Biologicals' combined diphtheria, tetanus, acellular pertussis-inactivated polio vaccine. <i>Meningitec™</i> (MenC): Wyeth's meningococcal serogroup C CRM₁₉₇ conjugated vaccine. <i>Pediacel™</i> (DTPa-IPV-Hib): Sanofi Pasteur MSD's combined diphtheria, tetanus, acellular pertussis-inactivated poliovirus- <i>Haemophilus influenzae</i> type b tetanus toxoid conjugate vaccine.</p>
<p>Phase: IV</p>
<p>Study Period: Hib-MenC-TT-027: 16 May 2007 to 12 October 2007. Hib-MenC-TT-028: 01 May 2008 to 24 September 2008.</p>
<p>Study Design: Open, multi-center, multi-country, non-randomized, long-term antibody persistence study with 3 groups.</p>
<p>Centers: Nine study centers: 1 center in the UK and 8 centers in Poland.</p>
<p>Indication: Immunization against <i>Haemophilus influenzae</i> type b and meningococcal serogroup C diseases and for subjects in the UK, against diphtheria, tetanus, pertussis and polio.</p>
<p>Treatment: The study groups were as follows:</p> <ul style="list-style-type: none"> ▪ HibMenC Group: primed in study 103974 with Hib-MenC (co-administered with DTPa-IPV) and boosted in study 104056 with Hib-MenC (co-administered with MMR). ▪ LicMenC Group: primed in study 103974 with MenC (co-administered with DTPa-IPV-Hib) and boosted in study 104056 with Hib-MenC (co-administered with MMR). ▪ NoBoost Group (only in the UK – enrolled at Visit 2): primed (according to the routine UK immunization schedule) with 3 doses of a MenC conjugate vaccine and a Hib containing vaccine before the age of 8 months without booster dose at 12 months of age. Those subjects received a catch-up dose of Hib-MenC in study 109666. <p>UK subjects in all 3 groups were boosted with DTPa-IPV vaccine at Visit 2 (study 109666) Note that at Visit 2, all subjects including those enrolled in the NoBoost Group were between 40 and 43 months of age.</p>
<p>Objectives: <i>In all evaluable subjects of groups HibMenC and LicMenC, at 12, 24 and 48 months after the Hib-MenC booster vaccination (i.e. at Visits 1, 2 & 3) and in all evaluable subjects of NoBoost Group at 40-43 months of age (i.e. at Visit 2):</i></p> <ul style="list-style-type: none"> ▪ To evaluate the persistence of meningococcal serogroup C antibodies. ▪ To evaluate the persistence of <i>Haemophilus influenzae</i> type b (Hib) antibodies. <p><i>In all UK evaluable subjects of HibMenC and LicMenC groups:</i></p> <ul style="list-style-type: none"> ▪ To evaluate the persistence of anti-pertussis antibodies prior to DTPa-IPV preschool booster and the response to DTPa-IPV preschool booster 24 months later.
<p>Primary Outcome/Efficacy Variable: Immunogenicity</p>

In all subjects of HibMenC and LicMenC groups, at Visit 1, Visit 2 and Visit 3 (i.e. at 12, 24 and 48+ months, respectively, after the Hib-MenC booster) and in all subjects of NoBoost Group at 40-43 months of age (i.e. at Visit 2):

- Serum bactericidal assay using baby rabbit complement (rSBA-MenC) titer $\geq 1:8$, $\geq 1:128$ and titers.
- Anti-polyribosyl-ribitol-phosphate (anti-PRP) antibody concentration $\geq 0.15 \mu\text{g/mL}$, $\geq 1.0 \mu\text{g/mL}$ and concentrations.
- Anti-polysaccharide C (anti-PSC) antibody concentration $\geq 0.30 \mu\text{g/mL}$, $\geq 2.0 \mu\text{g/mL}$ and concentrations.

In all UK subjects of HibMenC and LicMenC groups at Visit 2 (32 months post-Dose 3 of DTPa-containing vaccine primary vaccination, prior to DTPa-IPV booster) and at Visit 3+ (24 months after DTPa-IPV booster):

- Anti-filamentous haemagglutinin (anti-FHA), anti-pertactin (anti-PRN) and anti-pertussis toxoid (anti-PT) antibodies concentration $\geq 5 \text{ EL.U/mL}$ and concentrations.

Safety

In all subjects of HibMenC and LicMenC groups:

- Serious adverse events (SAEs) occurring from the last study contact of the booster study 104056 until the end of the persistence study*+.

*Note on retrospective recording of SAEs: at 12 and 24 months after booster vaccination the subject's parents/guardian were asked if any SAEs had occurred since the previous visits (i.e. since the last visit of the booster vaccination study 104056). Only those SAEs that were determined by the investigators to have a causal relationship to the booster vaccination were recorded and described individually, along with the nature of the SAEs and the outcomes. Any event related to lack of vaccine efficacy (meningococcal, Hib or pertussis medical/vaccine history were recorded) or related to study participation were recorded during the long-term persistence phase and were described in detail.

In UK subjects:

- Serious adverse events (SAEs) occurring within 31 days of administration of the DTPa-IPV (HibMenC, LicMenC and NoBoost groups) and Hib-MenC (NoBoost Group) vaccines**.

** Note on recording of SAEs after the DTPa-IPV and Hib-MenC vaccines: SAEs occurring within 31 days following the administration of the DTPa-IPV and Hib-MenC vaccines, whether assessed by the investigators as related or not, were recorded.

+Data until Month 24 are presented in this CTRS. The Month 48 data, not available when this summary was posted, will be disclosed when available

Outcome variables were not differentiated into primary and secondary in the study protocol, hence all were considered as primary outcome variables.

Secondary Outcome/Efficacy Variable(s): Not Applicable.

Statistical Methods:

The analyses were performed on the Total Cohort Year 1, the According-To-Protocol (ATP) cohort for persistence Year 1, the Total Cohort Year 2 and the ATP cohort for persistence Year 2.

- The Total Cohort Year 1 included all subjects who received the booster dose during study Hib-MenC-TT-012 BST:012 (104056) and came back for the Year 1 follow-up.
- The ATP cohort for persistence Year 1 included all evaluable subjects who received 3 doses of vaccines according to their random assignment during the vaccination study Hib-MenC-TT-012 (103974) and the corresponding booster doses in study 104056, who had available assay results for at least one tested antigen (rSBA-MenC, anti-PSC or anti-PRP), who had not received a previous booster dose of Hib, meningococcal serogroup C vaccines except study vaccines received during the booster study 104056 and who did not have a history of *Haemophilus influenzae* type b, meningococcal serogroup C diseases.
- The Total Cohort Year 2 included all vaccinated subjects in the booster study 104056 who came back for the year 2 follow-up and also all subjects of NoBoost Group who were enrolled and vaccinated at Visit 2 (i.e. 40-43 months of age).
- The ATP cohort for persistence Year 2 included for HibMenC and LicMenC groups all evaluable subjects who received 3 doses of vaccines according to their random assignment during the vaccination study 103974 and the corresponding booster doses in study 104056 and for the NoBoost Group all evaluable subjects who had received a 3-dose primary vaccination with a MenC conjugate vaccine and a Hib containing vaccine before the age of 8 months (without a MenC and Hib booster dose in the second year of life), who had assay results available for at least one tested antigen (rSBA-MenC, anti-PSC or anti-PRP [HibMenC, LicMenC and NoBoost groups] and , anti-PT, anti-FHA or anti-PRN [HibMenC and LicMenC groups in the UK]) at the Year 2 (Month 24) time point, who had not received a previous booster dose of Hib, meningococcal serogroup C vaccines except study vaccines received during the booster study 104056 (HibMenC and LicMenC groups) and who did not have a history of *Haemophilus influenzae* type b, meningococcal serogroup C diseases. In the UK only, evaluable subjects who had not received a previous administration of a booster dose of pertussis vaccine and who did not have a history of pertussis disease.

Analysis of meningococcal serogroup C and Hib antibody persistence:

The analysis of meningococcal serogroup C and Hib antibody persistence was based on the ATP cohort for persistence Year 1 and the ATP cohort for persistence Year 2.

In HibMenC and LicMenC groups, before the primary vaccination, one month post-dose 3, pre-booster (i.e. prior to Hib-MenC booster at 12-15 months of age), post-booster (i.e. one month after Hib-MenC booster), at Year 1 (Visit 1, i.e. 12 months after the Hib-MenC booster, at 24-31 months of age) and in all groups at Year 2 (Visit 2, i.e. 24 months after the Hib-MenC booster, at 40-43 months of age):

- Geometric mean antibody concentrations or titers (GMCs or GMTs) with 95% confidence intervals (CIs) were tabulated for anti-PRP, rSBA-MenC and anti-PSC antibodies. Antibody concentrations or titres below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC or GMT calculation.
- Seropositivity rates, seroprotection rates and percentages of subjects with titers or concentrations above proposed cut-offs with exact 95% CIs were calculated for anti-PRP, rSBA-MenC and anti-PSC antibodies.

Analysis of pertussis antibodies persistence (only for UK subjects in HibMenC and LicMenC groups):

The analysis of the persistence of pertussis antibodies was based on the ATP cohort for persistence Year 2 (HibMenC and LicMenC groups - UK subjects only).

Before the primary vaccination, at one month post-dose 3, at 8 months post-Dose 3 & prior to Hib-MenC booster (at 12-15 months of age) and at Year 2 (Visit 2, i.e. 32 months post-Dose 3 and 24 months after the Hib-MenC booster at 40-43 months of age): GMCs and percentage of subjects with antibody concentrations ≥ 5 EL.U/mL with 95% CIs were tabulated for anti-PT, anti-FHA and anti-PRN.

Analysis of Safety:

The analysis of safety was based on the Total Cohort Year 1 and Total Cohort Year 2.

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. For UK subjects, the number of subjects who reported at least one SAE following DTPa-IPV vaccine (in all 3 groups) and Hib-MenC vaccine (in NoBoost Group) booster dose was tabulated according to MedDRA preferred terms.

Study Population: Healthy male or female subjects between and including 24 and 31 months of age at Visit 1, between 40 and 43 months of age at the time of Visit 2, who had completed the booster vaccination study 104056 were included. For the NoBoost Group (UK only): healthy male and female children 40-43 months of age at Visit 2, who had been primed with 3 doses of a MenC conjugate vaccine and a Hib containing vaccine before the age of 8 months and who had not received a booster dose at 12 months of age were included.

Written informed consent was obtained from the parent or guardian of the subject prior to any study procedure.

Number of subjects in study 104056	HibMenC Group	LicMenC Group
Planned, N	375	125
Entered, N (Booster Total Vaccinated Cohort)	359	117
Completed, n (%)	357 (99.4)	116 (99.1)
Total Number Subjects Withdrawn, n (%)	2 (0.6)	1 (0.9)
Withdrawn due to Adverse Events, n (%)	1 (0.3)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	1 (0.3)	1 (0.9)
Demographics	HibMenC Group	LicMenC Group
N (Total Vaccinated Cohort)	359	117
Females: Males	179:180	62:55
Mean Age, months (SD)	12.8 (0.75)	12.8 (0.78)
White/Caucasian, n (%)	342 (95.3)	117 (100)
Number of subjects in study 109664	HibMenC Group	LicMenC Group
Planned, N	360	118
Entered, N (Total Cohort Year 1)	221	67
Completed, n (%)	221 (100)	67 (100)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	0 (0.0)
Demographics	HibMenC Group	LicMenC Group
N (Total Cohort Year 1)	221	67
Females:Males	114:107	33:34
Mean Age, months (SD)	27.9 (0.97)	27.7 (0.68)

White/Caucasian, n (%)	216 (97.7)		67 (100)
Number of subjects in study 109666	HibMenC Group	LicMenC Group	NoBoost Group
Planned, N	360	118	75
Entered, N (Total Cohort Year 2)	235	77	74
Completed, n (%)	235 (100)	77 (100)	74 (100)
Total Number Subjects Withdrawn, n (%)	Not applicable	Not applicable	Not applicable
Demographics	HibMenC Group	LicMenC Group	NoBoost Group
N (Total Cohort Year 2)	235	77	74
Females: Males	117:118	37:40	28:46
Mean Age, months (SD)	40.6 (0.76)	40.6 (0.74)	40.5 (0.71)
White/Caucasian/European heritage, n (%)	228 (97.0)	77 (100)	68 (94.4)

Primary Efficacy Results:

Percentage of subjects with titer $\geq 1:8$ or $\geq 1:128$ and GMTs for rSBA-MenC antibodies (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	HibMenC	Pre-Primary	204	12	5.9	3.1	10.0	3	1.5	0.3	4.2	4.8	4.3	5.3
		Post-Primary	202	200	99.0	96.5	99.9	189	93.6	89.2	96.5	624.7	530.7	735.4
		Pre-Booster	202	163	80.7	74.6	85.9	94	46.5	39.5	53.7	67.1	52.8	85.3
		Post-Booster	203	201	99.0	96.5	99.9	199	98.0	95.0	99.5	2540.3	2058.0	3135.5
		PIV (M12)	200	178	89.0	83.8	93.0	109	54.5	47.3	61.5	123.0	98.9	153.0
	LicMenC	Pre-Primary	60	3	5.0	1.0	13.9	0	0.0	0.0	6.0	4.3	3.9	4.8
		Post-Primary	63	63	100	94.3	100	63	100	94.3	100	1000.0	778.8	1284.2
		Pre-Booster	62	39	62.9	49.7	74.8	19	30.6	19.6	43.7	32.4	20.3	51.6
		Post-Booster	64	61	95.3	86.9	99.0	56	87.5	76.8	94.4	517.4	346.7	772.0
		PIV (M12)	59	41	69.5	56.1	80.8	17	28.8	17.8	42.1	35.7	23.4	54.5

GMT = geometric mean antibody titer calculated on all subjects

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-Primary = pre primary vaccination

Post-Primary = one month post primary dose 3

Pre-Booster = pre booster dose

Post-Booster = one month post booster dose

PIV(M12) = 12 months after booster vaccination

Primary Efficacy Results:

Percentage of subjects with titer $\geq 1:8$ or $\geq 1:128$ and GMTs for rSBA-MenC antibodies (ATP cohort for persistence Year 2)

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	HibMenC	Pre-Primary	227	16	7.0	4.1	11.2	5	2.2	0.7	5.1	5.0	4.4	5.6
		Post-Primary	224	222	99.1	96.8	99.9	208	92.9	88.7	95.9	592.3	507.3	691.5
		Pre-Boost	226	175	77.4	71.4	82.7	96	42.5	35.9	49.2	58.6	46.4	73.9
		Post-Boost (M1)	228	227	99.6	97.6	100	225	98.7	96.2	99.7	2320.8	1926.2	2796.2
		Post-Boost (M12)	184	164	89.1	83.7	93.2	98	53.3	45.8	60.6	122.3	97.5	153.4
		Post-Boost (M24)	219	147	67.1	60.5	73.3	86	39.3	32.8	46.1	48.0	36.8	62.6
	LicMenC	Pre-Primary	70	2	2.9	0.3	9.9	0	0.0	0.0	5.1	4.2	3.9	4.5
		Post-Primary	73	73	100	95.1	100	73	100	95.1	100	1075.6	859.8	1345.5
		Pre-Boost	72	48	66.7	54.6	77.3	22	30.6	20.2	42.5	35.0	23.1	53.0
		Post-Boost (M1)	76	73	96.1	88.9	99.2	66	86.8	77.1	93.5	520.9	367.9	737.6
		Post-Boost (M12)	53	37	69.8	55.7	81.7	15	28.3	16.8	42.3	35.9	22.9	56.0
		Post-Boost (M24)	74	30	40.5	29.3	52.6	10	13.5	6.7	23.5	14.4	9.7	21.6

	NoBoost	Aged 40-43 mths	68	30	44.1	32.1	56.7	11	16.2	8.4	27.1	15.9	10.3	24.3
GMT = geometric mean antibody titer calculated on all subjects 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-primary = Pre-primary vaccination Post-primary = One month after the primary vaccination Pre-Boost = Pre-booster vaccination Post-Boost (M1) = One month after the booster vaccination Post-Boost (M12) = 12 Months after the booster vaccination (24 – 31 months of age) Post-Boost (M24) = 24 Months after the booster vaccination (40 – 43 months of age) Aged 40-43 mths: subjects in NoBoost were 40 to 43 months of age (i.e. age-matched with the children from HibMenC and LicMenC groups at the moment of Visit 2 [i.e. 24 months post Hib-MenC booster vaccination]).														
Primary Efficacy Results:														
Percentage of subjects with concentrations $\geq 0.15 \mu\text{g/mL}$ or $1.0 \mu\text{g/mL}$ and GMCs for anti-PRP antibodies (ATP cohort for persistence Year 1)														
Antibody	Group	Timing	N	$\geq 0.15 \mu\text{g/mL}$				$\geq 1 \mu\text{g/mL}$				GMC ($\mu\text{g/mL}$)		
				n	%	95% CI		n	%	95% CI		Value	95% CI	
						LL	UL			LL	UL		LL	UL
Anti-PRP	HibMenC	Pre-Primary	206	84	40.8	34.0	47.8	20	9.7	6.0	14.6	0.160	0.137	0.186
		Post-Primary	204	204	100	98.2	100	198	97.1	93.7	98.9	12.413	10.688	14.417
		Pre-Booster	204	199	97.5	94.4	99.2	120	58.8	51.7	65.6	1.293	1.095	1.528
		Post-Booster	203	203	100	98.2	100	203	100	98.2	100	88.667	74.609	105.373
		PIV (M12)	198	198	100	98.2	100	188	94.9	90.9	97.6	7.153	6.029	8.486
	LicMenC	Pre-Primary	63	25	39.7	27.6	52.8	11	17.5	9.1	29.1	0.178	0.130	0.243
		Post-Primary	63	58	92.1	82.4	97.4	43	68.3	55.3	79.4	2.473	1.557	3.928
		Pre-Booster	64	45	70.3	57.6	81.1	19	29.7	18.9	42.4	0.441	0.309	0.627
		Post-Booster	63	63	100	94.3	100	63	100	94.3	100	39.024	30.588	49.786
		PIV (M12)	63	63	100	94.3	100	52	82.5	70.9	90.9	3.162	2.316	4.318
GMC = geometric mean antibody concentration calculated on all subjects 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-Primary = pre primary vaccination Post-Primary = one month post primary dose 3 Pre-Booster = pre booster dose Post-Booster = one month post booster dose PIV(M12) = 12 months after booster vaccination														
Primary Efficacy Results:														
Percentage of subjects with concentration $\geq 0.15 \mu\text{g/mL}$ or $1.0 \mu\text{g/mL}$ and GMCs for anti-PRP antibodies (ATP cohort for persistence Year 2)														
Antibody	Group	Timing	N	$\geq 0.15 \mu\text{g/mL}$				$\geq 1 \mu\text{g/mL}$				GMC ($\mu\text{g/mL}$)		
				n	%	95% CI		n	%	95% CI		value	95% CI	
						LL	UL			LL	UL		LL	UL
Anti-PRP	HibMenC	Pre-Primary	230	93	40.4	34.0	47.1	18	7.8	4.7	12.1	0.153	0.134	0.176
		Post-Primary	227	227	100	98.4	100	222	97.8	94.9	99.3	12.794	11.159	14.669
		Pre-Boost	229	222	96.9	93.8	98.8	134	58.5	51.8	65.0	1.260	1.080	1.469
		Post-Boost (M1)	228	228	100	98.4	100	228	100	98.4	100	91.981	78.700	107.503
		Post-Boost (M12)	182	182	100	98.0	100	172	94.5	90.1	97.3	7.107	5.931	8.516
		Post-Boost (M24)	228	227	99.6	97.6	100	203	89.0	84.2	92.8	4.790	4.065	5.644
	LicMenC	Pre-Primary	73	30	41.1	29.7	53.2	9	12.3	5.8	22.1	0.163	0.125	0.213
		Post-Primary	73	66	90.4	81.2	96.1	52	71.2	59.4	81.2	2.396	1.580	3.635
		Pre-Boost	74	53	71.6	59.9	81.5	21	28.4	18.5	40.1	0.425	0.310	0.582
		Post-Boost (M1)	75	75	100	95.2	100	75	100	95.2	100	44.002	34.546	56.048
		Post-Boost (M12)	57	57	100	93.7	100	48	84.2	72.1	92.5	3.456	2.488	4.799

		Post-Boost (M24)	75	74	98.7	92.8	100	56	74.7	63.3	84.0	2.339	1.798	3.042
	NoBoost	Aged 40-43 mths	72	62	86.1	75.9	93.1	28	38.9	27.6	51.1	0.668	0.467	0.956
<p>GMC = geometric mean antibody concentration calculated on all subjects 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-primary = Pre-primary vaccination Post-primary = One month after the primary vaccination Pre-Boost = Pre-booster dose Post-Boost (M1) = One month after the booster vaccination Post-Boost (M12) = 12 Months after the booster vaccination (24-31 months of age) Post-Boost (M24) = 24 Months after the booster vaccination (40-43 months of age) Aged 40-43 mths: subjects in NoBoost were 40 to 43 months of age (i.e. age-matched with the children from HibMenC and LicMenC groups at the moment of Visit 2 [i.e. 24 months post Hib-MenC booster vaccination]).</p>														
Primary Efficacy Results:														
Percentage of subjects with concentrations $\geq 0.3 \mu\text{g/mL}$ or $2 \mu\text{g/mL}$ and GMCs for anti-PSC antibodies (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	HibMenC	Pre-Primary	206	19	9.2	5.6	14.0	8	3.9	1.7	7.5	0.18	0.17	0.20
		Post-Primary	202	202	100	98.2	100	201	99.5	97.3	100	9.52	8.68	10.45
		Pre-Booster	201	170	84.6	78.8	89.3	27	13.4	9.0	18.9	0.77	0.67	0.88
		Post-Booster	205	205	100	98.2	100	183	89.3	84.2	93.2	7.36	6.46	8.39
		PIV (M12)	193	119	61.7	54.4	68.5	19	9.8	6.0	14.9	0.47	0.40	0.55
	LicMenC	Pre-Primary	63	4	6.3	1.8	15.5	1	1.6	0.0	8.5	0.17	0.15	0.18
		Post-Primary	63	63	100	94.3	100	63	100	94.3	100	11.20	9.42	13.33
		Pre-Booster	64	56	87.5	76.8	94.4	10	15.6	7.8	26.9	0.84	0.66	1.06
		Post-Booster	64	64	100	94.4	100	47	73.4	60.9	83.7	3.51	2.84	4.32
		PIV (M12)	59	29	49.2	35.9	62.5	2	3.4	0.4	11.7	0.32	0.26	0.40
<p>GMC = geometric mean antibody concentration calculated on all subjects 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-Primary = pre primary vaccination Post-Primary = one month post primary dose 3 Pre-Booster = pre booster dose Post-Booster = one month post booster dose PIV(M12) = 12 months after booster vaccination</p>														
Primary Efficacy Results:														
Percentage of subjects with concentrations $\geq 0.3 \mu\text{g/mL}$ or $2 \mu\text{g/mL}$ and GMCs for anti-PSC antibodies (ATP cohort for persistence Year 2)														
Antibody	Group	Timing	N	$\geq 0.3 \mu\text{g/mL}$				$\geq 2.0 \mu\text{g/mL}$				GMC ($\mu\text{g/mL}$)		
				n	%	95% CI		n	%	95% CI		Value	95% CI	
						LL	UL			LL	UL		LL	UL
Anti-PSC	HibMenC	Pre-Primary	229	26	11.4	7.6	16.2	12	5.2	2.7	9.0	0.20	0.18	0.22
		Post-Primary	225	225	100	98.4	100	224	99.6	97.5	100	9.35	8.56	10.22
		Pre-Boost	226	188	83.2	77.7	87.8	27	11.9	8.0	16.9	0.74	0.65	0.84
		Post-Boost (M1)	230	230	100	98.4	100	210	91.3	86.9	94.6	7.41	6.59	8.33
		Post-Boost (M12)	178	110	61.8	54.2	69.0	16	9.0	5.2	14.2	0.47	0.40	0.55
		Post-Boost (M24)	226	76	33.6	27.5	40.2	5	2.2	0.7	5.1	0.25	0.23	0.28
	LicMenC	Pre-Primary	73	6	8.2	3.1	17.0	1	1.4	0.0	7.4	0.17	0.15	0.18
		Post-Primary	72	72	100	95.0	100	72	100	95.0	100	12.29	10.50	14.39
		Pre-Booster	74	66	89.2	79.8	95.2	13	17.6	9.7	28.2	0.87	0.69	1.10
		Post-Booster (M1)	76	76	100	95.3	100	59	77.6	66.6	86.4	3.91	3.19	4.79

		Post-Booster (M12)	54	26	48.1	34.3	62.2	2	3.7	0.5	12.7	0.32	0.25	0.40
		Post-Booster (M24)	75	17	22.7	13.8	33.8	0	0.0	0.0	4.8	0.21	0.18	0.24
	NoBoost	Aged 40-43 mths	72	4	5.6	1.5	13.6	0	0.0	0.0	5.0	0.16	0.15	0.18
<p>GMC = geometric mean antibody concentration calculated on all subjects 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-primary = Pre-primary vaccination Post-primary = One month after the primary vaccination Pre-Booster = Pre-booster dose Post-Booster (M1) = One month after the booster vaccination Post-Booster (M12) = 12 Months after the booster vaccination (24-31 months of age) Post-Booster (M24) = 24 Months after the booster vaccination (40 – 43 months of age) Aged 40-43 mths: subjects in NoBoost were 40 to 43 months of age (i.e. age-matched with the children from HibMenC and LicMenC groups at the moment of Visit 2 [i.e. 24 months post Hib-MenC booster vaccination]).</p>														
Primary Efficacy Results:														
Percentage of subjects with concentration ≥ 5.0 EL.U/mL and GMCs for Anti-PT, Anti-FHA and Anti-PRN antibodies, on all UK subjects of HibMenC and LicMenC groups (ATP cohort for persistence Year 2)														
Antibody	Group	Timing	N	≥ 5 EL.U/mL				GMC (EL.U/mL)						
				n	%	95% CI		Value	95% CI					
						LL	UL		LL	UL				
Anti-PT	HibMenC	Pre-Primary	64	11	17.2	8.9	28.7	3.2	2.8	3.7				
		Post-Primary (M1)	63	63	100	94.3	100	44.8	39.1	51.2				
		Post-Primary (M8)	66	34	51.5	38.9	64.0	4.9	4.1	5.9				
		Pre-Boost	67	8	11.9	5.3	22.2	2.9	2.6	3.2				
	LicMenC	Pre-Primary	18	3	16.7	3.6	41.4	3.3	2.4	4.6				
		Post-Primary (M1)	20	20	100	83.2	100	40.1	31.7	50.8				
		Post-Primary (M8)	21	10	47.6	25.7	70.2	4.5	3.3	6.1				
		Pre-Boost	23	3	13.0	2.8	33.6	3.0	2.4	3.6				
Anti-FHA	HibMenC	Pre-Primary	65	40	61.5	48.6	73.3	6.5	5.2	8.2				
		Post-Primary (M1)	63	63	100	94.3	100	223.5	194.6	256.7				
		Post-Primary (M8)	65	65	100	94.5	100	30.4	25.7	35.9				
		Pre-Boost	64	47	73.4	60.9	83.7	15.1	9.5	24.0				
	LicMenC	Pre-Primary	19	12	63.2	38.4	83.7	7.8	4.7	13.0				
		Post-Primary (M1)	20	20	100	83.2	100	160.2	123.1	208.6				
		Post-Primary (M8)	21	21	100	83.9	100	25.8	19.0	34.9				
		Pre-Boost	22	13	59.1	36.4	79.3	20.3	8.0	51.8				
Anti-PRN	HibMenC	Pre-Primary	64	22	34.4	22.9	47.3	4.2	3.4	5.2				
		Post-Primary (M1)	63	63	100	94.3	100	116.3	93.7	144.5				
		Post-Primary (M8)	66	53	80.3	68.7	89.1	12.5	9.5	16.2				
		Pre-Boost	67	34	50.7	38.2	63.2	5.9	4.5	7.7				
	LicMenC	Pre-Primary	19	4	21.1	6.1	45.6	3.1	2.5	3.9				
		Post-Primary (M1)	20	20	100	83.2	100	46.1	31.0	68.5				
		Post-Primary (M8)	21	14	66.7	43.0	85.4	6.6	4.4	9.9				
		Pre-Boost	23	7	30.4	13.2	52.9	4.3	2.8	6.5				
<p>GMC = geometric mean antibody concentration calculated on all subjects 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-primary = Pre-primary vaccination Post-primary (M1) = one month after the primary vaccination Post-primary (M8) = eight months after primary vaccination Pre-Boost = before DTPa-IPV booster vaccination</p>														
Secondary Outcome Variable(s): Not Applicable.														
Safety results: Number (%) of subjects with related serious adverse events determined by the investigators to have														

causal relationship to vaccination until 12 months after Hib-MenC booster vaccination (Total Cohort Year 1)			
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]			
All SAEs	HibMenC Group N = 359	LicMenC Group N = 117	
Subjects with any SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	
Fatal SAEs	HibMenC Group N = 359	LicMenC Group N = 117	
Subjects with fatal SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	
Safety results: Number (%) of subjects with related serious adverse events determined by the investigators to have causal relationship to vaccination until 24 months after Hib-MenC booster vaccination (Total Cohort Year 2)			
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]			
All SAEs	HibMenC Group N = 359	LicMenC Group N = 117	
Subjects with any SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	
Fatal SAEs	HibMenC Group N = 359	LicMenC Group N = 117	
Subjects with fatal SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	
Safety results: Number (%) of subjects with serious adverse events following DTPa-IPV (and Hib-MenC for NoBoost Group) vaccinations during the 31-day follow-up period, in all UK subjects (Total cohort Year 2)			
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]			
All SAEs	HibMenC Group N = 70	LicMenC Group N = 23	NoBoost Group N = 72
Subjects with any SAE(s), n (%) [n related]	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Asthma	1 (1.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	HibMenC Group	LicMenC Group	NoBoost Group
Subjects with fatal SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

Conclusion: Twelve months after the Hib-MenC booster vaccination 89.0% of the subjects in the HibMenC Group and 69.5% of the subjects in the LicMenC Group had rSBA-MenC antibody titer $\geq 1:8$; all subjects in both groups had anti-PRP antibody concentration $\geq 0.15 \mu\text{g/mL}$.

Twenty-four months after the Hib-MenC booster vaccination, 67.1% of subjects in the HibMenC Group and 40.5% subjects in the LicMenC Group had rSBA-MenC antibody titer $\geq 1:8$; 99.6% of subjects in HibMenC Group and 98.7% in LicMenC Group had anti-PRP antibody concentrations $\geq 0.15 \mu\text{g/mL}$.

At the same time point (i.e. about 3 years after DTPa-IPV 3-dose primary vaccination) in the UK subjects of the HibMenC Group, 11.9%, 73.4% and 50.7% had anti-PT, anti-FHA and anti-PRN antibodies $\geq 5\text{EL.U/mL}$, respectively; in the UK subjects of the LicMenC Group, 13.0%, 59.1% and 30.4% had anti-PT, anti-FHA and anti-PRN antibodies $\geq 5\text{EL.U/mL}$, respectively.

During the 31-day follow-up after vaccination (DTPa-IPV, [and Hib-MenC in NoBoost Group]), one SAE was reported for one UK subject in the HibMenC Group; it was not considered by the investigator to be related with the study vaccination. No fatal SAEs were reported up to Month 24 post Hib-MenC booster vaccination.

For safety results on the primary vaccination and booster studies, please refer to 103974 and 104056 CTRS. Please refer also to the publication below.

Publications:

Khatami A et al. Persistence of antibody response following a booster dose of Hib-MenC-TT glycoconjugate vaccine: A phase IV open randomized controlled trial. Abstract presented at the 27th annual ESPID meeting, Brussels, Belgium, 9-13 June 2009.

Date updated: 28-Sep-2009