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| Study No.: 104056 (Hib-MenC-TT-013 BST:012) |
| Title: A phase III open (partially double-blind), controlled, multicenter, multicountry primary and booster vaccination study to demonstrate the non-inferiority of the meningococcal serogroup C immune response of GlaxoSmithKline (GSK) Biologicals' Hib-MenC vaccine co-administered with Infanrix™ IPV versus a licensed meningococcal serogroup C vaccine co-administered with Pediacel™ when given according to a 2, 3, 4 month schedule and the immunogenicity of the Hib-MenC vaccine when given as a booster dose at 12-15 months of age. Hib-MenC (Menitorix): GlaxoSmithKline (GSK) Biologicals' <i>Haemophilus influenzae</i> type b (Hib) – meningococcal serogroup C (MenC) tetanus toxoid conjugate vaccine. Infanrix™ IPV (DTPa-IPV): GSK Biologicals' combined diphtheria, tetanus, acellular pertussis, inactivated polio vaccine. Meningitec™ Lic-MenC): Wyeth's licensed meningococcal serogroup C conjugate vaccine. Pediacel™ (DTPa-IPV/Hib): Sanofi Pasteur's combined diphtheria, tetanus, acellular pertussis, inactivated polio and <i>Haemophilus influenzae</i> type b vaccine. |
| Rationale: The aim was to evaluate the immunogenicity and safety of a booster dose of the Hib-MenC vaccine co-administered with MMR vaccine at 12 to 15 months of age as well as the persistence of antibodies following primary vaccination. This study was conducted in 2 parts: the primary vaccination phase 103974 (HIB-MENC-TT-012) and the booster phase 104056 (HIB-MENC-TT-013 BST: 012). This CTRS report presents the results of the booster phase of the study. The results of the primary vaccination phase are presented in a separate document. Priorix™ (MMR): GSK Biologicals' combined measles, mumps and rubella vaccine. |
| Phase: III |
| Study Period: 02 February 2006 to 13 July 2006 |
| Study Design: Open randomized (3:1), multi-centre, multi-country study with 2 study groups. |
| Centers: 10 study centers (1 in the UK and 9 in Poland). |
| Indication: Booster vaccination of healthy infants against <i>Haemophilus influenzae</i> type b and meningococcal serogroup C diseases |
| Treatment: The study groups in this booster phase were as follows: <ul style="list-style-type: none"> • HibMenC Group: subjects primed with Hib-MenC co-administered with DTPa-IPV and boosted with Hib-MenC co-administered with MMR. • LicMenC Group: subjects primed with Lic-MenC co-administered with DTPa-IPV/Hib and boosted with Hib-MenC co-administered with MMR. Hib-MenC vaccine was administered by intramuscular injection into the right deltoid region while MMR vaccine was injected subcutaneously in the left upper arm in toddlers aged 12 months. For some data analyses, the 2 groups were pooled into Pooled Group. |
| Objectives: <ul style="list-style-type: none"> • 42 days after the booster vaccination, to evaluate the immunogenicity in terms of the percentage of subjects with serum bactericidal assay using rabbit complement (rSBA)-MenC titers $\geq 1:128$ induced by a booster dose of Hib-MenC vaccine given concomitantly with MMR vaccine in toddlers aged 12 to 15 months who had been primed with either 3 doses of DTPa-IPV and Hib-MenC vaccines or DTPa-IPV/Hib and Lic-MenC vaccines. (Criteria for success: Lower limit of the exact 95% CI on the percentage of subjects with rSBA-MenC titres $\geq 1:128$ in the Hib-MenC group above 90%.) • 42 days after the booster vaccination, to evaluate the immunogenicity in terms of the percentage of subjects with anti-polyribosylribitol phosphate (anti-PRP) antibody concentration ≥ 1.0 $\mu\text{g/mL}$ induced by a booster dose of Hib-MenC vaccine given concomitantly with MMR vaccine in toddlers aged 12 to 15 months who had been primed with either 3 doses of DTPa- |

IPV and Hib-MenC vaccines or DTPa-IPV/Hib and Lic-MenC vaccines.
(Criteria for success: Lower limit of the exact 95% CI on the percentage of subjects with anti-PRP concentration $\geq 1\mu\text{g/mL}$ in the Hib-MenC group above 90%.)

Primary Outcome/Efficacy Variable:

42 days after the booster vaccination:

- rSBA-MenC titer $\geq 1:128$
- Anti-PRP antibody concentration $\geq 1\mu\text{g/mL}$

Secondary Outcome/Efficacy Variable(s):

Immunogenicity

Prior to the booster vaccination (persistence):

- rSBA-MenC antibody titer $\geq 1:8$ and $\geq 1:128$ and titers
- Anti-meningococcal serogroup C polysaccharide (anti-PSC) antibody concentration $\geq 0.30\mu\text{g/mL}$ & $\geq 2\mu\text{g/mL}$ and concentrations
- Anti-PRP antibody concentration $\geq 0.15\mu\text{g/mL}$ & $\geq 1\mu\text{g/mL}$ and concentrations
- Anti-measles antibody concentration $\geq 150\text{mIU/mL}$ and concentrations
- Anti-mumps antibody concentration $\geq 231\text{IU/mL}$ and concentrations
- Anti-rubella antibody concentration $\geq 4\text{IU/mL}$ and concentrations
- Anti-diphtheria antibody concentration $\geq 0.1\text{IU/mL}$ and concentrations
- Anti-tetanus antibody concentration $\geq 0.1\text{IU/mL}$ and concentrations
- Anti-polio type 1, 2 and 3 antibody titer ≥ 8 and titers
- Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA), and anti-pertactin (anti-PRN) antibody concentration $\geq 5\text{EL.U/mL}$ and concentrations

42 days after booster vaccination:

- rSBA-MenC antibody titer $\geq 1:8$ and titers
- Anti-PSC antibody concentration $\geq 0.30\mu\text{g/mL}$ and $\geq 2\mu\text{g/mL}$ and concentrations
- Anti-PRP antibody concentration $\geq 0.15\mu\text{g/mL}$ and concentrations
- Anti-measles antibody concentration $\geq 150\text{mIU/mL}$, seroconversion* rates and concentrations
- Anti-mumps antibody concentration $\geq 231\text{IU/mL}$, seroconversion* rates and concentrations
- Anti-rubella antibody concentration $\geq 4\text{IU/mL}$, seroconversion* rates and concentrations

*Seroconversion to measles, mumps or rubella was defined as the appearance of antibodies to the relevant antibody (i.e. titer \geq cut-off value) in the serum of subjects who were seronegative (i.e. with titre <cut-off value) for that antibody before vaccination

Safety

- Occurrence of local solicited adverse events (AEs) during the solicited follow-up period (Day 0–3) following the administration of the booster dose
- Occurrence of solicited general AEs, during the solicited follow-up period (Day 03) following the administration of the booster dose.
- Occurrence of unsolicited non-serious AEs within 30 days after booster vaccination.
- Occurrence of MMR specific solicited general AEs during the 43-day period (Day 0–42) after the booster dose.
- Occurrence of any serious adverse events (SAEs) throughout the study.

Statistical Methods:

The analyses were performed on the Booster Total Vaccinated cohort, the According-To-Protocol (ATP) cohort for antibody persistence and the Booster ATP cohort for immunogenicity.

The Booster Total Vaccinated cohort included all vaccinated subjects for whom data for the booster phase were available.

The ATP cohort for antibody persistence included all vaccinated subjects who received the 3 vaccine doses in the primary vaccination course and had not received a vaccine not specified or forbidden in the protocol.

The Booster ATP cohort for immunogenicity included all subjects who received the 3 vaccine doses in the primary vaccine course and the *booster vaccine dose*, who had not received a vaccine not specified or forbidden in the protocol, who met all eligibility criteria and *for whom assay results were*

available.

Analysis of immunogenicity

For antibody persistence

The analysis of immunogenicity was performed on the ATP cohort for antibody persistence (blood samples taken at Study Month 10, i.e. when the child was aged of 12 months).

Seropositivity or seroprotection rates and geometric mean antibody concentrations (GMCs) or geometric mean titers (GMTs) were tabulated for rSBA-MenC, anti-PRP, anti-PSC, anti-diphtheria, anti-tetanus, anti-polio types 1, 2 & 3, anti-PT, anti-FHA and anti-PRN antibodies one month after the primary vaccination course and before the booster vaccination with 95% confidence interval (CI) for each group.

For the immune response

The analysis was performed on the Booster ATP cohort for immunogenicity (blood samples taken at Study Month 11.5, i.e. 42 days after the booster dose).

Seropositivity, seroprotection or seroconversion rates and GMCs or GMTs were tabulated for rSBA-MenC, anti-PRP, anti-PSC, anti-measles, anti-mumps and anti-rubella antibodies at pre- and post-booster vaccination with 95% CI for each group and for pooled group. As the booster phase of the study was an extension of the primary vaccination phase, the primary objectives of the booster vaccination phase were considered conclusive only if all the primary objectives of the primary vaccination phase were reached, which was the case (see CTRS for 103974 (HIB-MENC-TT-012)). The co-primary objectives of the booster phase were assessed in a sequential fashion i.e. a conclusion was drawn on the second objective only if the first objective had been demonstrated. The objectives were met if, for the pooled groups, the lower limits of the exact 95% CI of the subjects with rSBA-MenC antibody titer $\geq 1:128$ and with PRP-antibody concentration $\geq 1 \mu\text{g/mL}$ were above 90%.

Analysis of safety

The analysis of safety was performed on the Booster Total Vaccinated cohort.

For each solicited symptom, the percentage of subjects with the symptom reported during the 4-day (Day 0-3) follow-up period after booster dose was summarized with exact 95% CI for each group and the Pooled Group.

The percentage of subjects with MMR specific solicited symptoms occurring during the 43-day follow-up period after the booster vaccination was tabulated.

The percentage of subjects reporting unsolicited AEs within 31 days (Day 0-30) following vaccine dose was tabulated according to the Medical Dictionary for Regulatory Activities (MedDRA) preferred term for each group and the Pooled Group.

The occurrence of SAEs was tabulated according to the MedDRA preferred terms for each group and the Pooled Group since the end of the primary phase and before the start of the booster vaccination and from the start of the booster vaccination until the end of the study.

Study Population: Male or female subjects who had participated in the primary vaccination phase 103974 (HIB-MENC-TT-012). Subjects with a history of measles, mumps, rubella, Hib and/or meningococcal serogroup C disease or with known exposure to measles, mumps or rubella within 30 days prior to start of the booster part were excluded. Subjects having received a previous vaccination against measles, mumps or rubella, a booster vaccination with a Hib vaccine or a serogroup C meningococcal vaccine were excluded. Written informed consent was obtained from the subjects' parent/guardian prior to entry into the primary study.

| Number of subjects | 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 | LicMenC Group |

| | | 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) | | | | | | | | | |
| Primary Efficacy Results: | | | | | | | | | | | | | |
| Immune response: percentage of subjects with antibody titer $\geq 1:8$ or $\geq 1:128$ and GMTs for rSBA-MenC antibodies, pre- and post-booster vaccination (Booster ATP cohort for immunogenicity) | | | | | | | | | | | | | |
| 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 |
| HibMen C | PiII(M10) | 34 | 26 | 77.9 | 73. | 82. | 14 | 43.8 | 38.5 | 49.3 | 61.0 | 50.6 | 73.5 |
| | PIV(M11.5) | 34 | 34 | 99.1 | 97. | 99. | 33 | 97.7 | 95.5 | 99.0 | 2193.7 | 1881.1 | 2558.1 |
| LicMen C | PiII(M10) | 10 | 74 | 67.9 | 58. | 76. | 36 | 33.0 | 24.3 | 42.7 | 38.6 | 27.5 | 54.2 |
| | PIV(M11.5) | 11 | 10 | 95.6 | 90. | 98. | 98 | 86.0 | 78.2 | 91.8 | 477.9 | 357.3 | 639.2 |
| Pooled | PiII(M10) | 44 | 33 | 75.5 | 71. | 79. | 18 | 41.2 | 36.6 | 45.9 | 54.6 | 46.3 | 64.3 |
| | PIV(M11.5) | 46 | 45 | 98.3 | 96. | 99. | 43 | 94.8 | 92.4** | 96.6 | 1504.9 | 1297.3 | 1745.7 |

N = number of subjects with available results
n (%) = number (percentage) of subjects with rSBA-MenC antibody titers within the specified range
PiII(M10) = pre-booster blood sample at Month 10
PIV(M11.5) = post-booster blood sample at Month 11.5
95% CI = 95% confidence interval; LL = lower limit; UL = upper limit
* Primary efficacy result
**co-primary objective was demonstrated as lower limit was above 90%

| Primary Efficacy Results: | | | | | | | | | | | | | |
|---|------------|-----|----------------------------|------|--------|-----|---------------------------|------|--------|------|--------------------------|--------|---------|
| Immune response: seroprotection rates and GMCs for anti-PRP antibodies, pre- and post-booster vaccination (Booster ATP cohort for immunogenicity) | | | | | | | | | | | | | |
| 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 |
| HibMen C | PiII(M10) | 344 | 33 | 96.5 | 94. | 98. | 21 | 61.3 | 56.0 | 66.5 | 1.352 | 1.189 | 1.538 |
| | PIV(M11.5) | 347 | 34 | 100 | 98. | 100 | 34 | 100* | 98.9 | 100 | 93.19 | 82.173 | 105.686 |
| LicMen C | PiII(M10) | 110 | 81 | 73.6 | 64. | 81. | 34 | 30.9 | 22.4 | 40.4 | 0.471 | 0.360 | 0.617 |
| | PIV(M11.5) | 114 | 11 | 100 | 96. | 100 | 11 | 100* | 96.8 | 100 | 44.26 | 36.769 | 53.295 |
| Pooled | PiII(M10) | 454 | 41 | 91.0 | 87. | 93. | 24 | 54.0 | 49.3 | 58.6 | 1.047 | 0.925 | 1.186 |
| | PIV(M11.5) | 461 | 46 | 100 | 99. | 100 | 46 | 100* | 99.2 | 100 | 77.52 | 69.520 | 86.447 |

N = number of subjects with available results
n (%) = number (percentage) of subjects with anti-PRP antibody concentrations within the specified range
PiII(M10) = pre-booster blood sample at Month 10
PIV(M11.5) = post-booster blood sample at Month 11.5

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

* Primary efficacy result

**co-primary objective was demonstrated as lower limit was above 90%

Secondary Outcome Variable (s):

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

| 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 |
| HibMen C | PIII(M3) | 347 | 344 | 99.1 | 97.5 | 99.8 | 321 | 92.5 | 89.2 | 95.0 | 575.3 | 508.4 | 651.0 |
| | PIII(M10) | 346 | 270 | 78.0 | 73.3 | 82.3 | 152 | 43.9 | 38.6 | 49.3 | 61.3 | 50.9 | 73.7 |
| LicMen C | PIII(M3) | 112 | 112 | 100 | 96.8 | 100 | 111 | 99.1 | 95.1 | 100 | 1005.7 | 834.4 | 1212.2 |
| | PIII(M10) | 109 | 74 | 67.9 | 58.3 | 76.5 | 36 | 33.0 | 24.3 | 42.7 | 38.6 | 27.5 | 54.2 |

N = number of subjects with available results

n (%) = number (percentage) of subjects with rSBA-MenC antibody titers within the specified range

PIII(M3) = post-Dose 3 blood sample at Month 3

PIII(M10) = pre-booster blood sample at Month 10

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

Secondary Outcome Variable (s):

Persistence: seroprotection rates 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 ($\mu\text{g/mL}$) | | |
|-------------|-----------|-----|----------------------------|------|--------|------|-------------------------|------|--------|------|--------------------------|--------|--------|
| | | | n | % | 95% CI | | n | % | 95% CI | | Value | 95% CI | |
| | | | | | LL | UL | | | LL | UL | | LL | UL |
| HibMen C | PIII(M3) | 350 | 350 | 100 | 99.0 | 100 | 341 | 97.4 | 95.2 | 98.8 | 13.025 | 11.631 | 14.586 |
| | PIII(M10) | 350 | 338 | 96.6 | 94.1 | 98.2 | 214 | 61.1 | 55.8 | 66.3 | 1.354 | 1.192 | 1.538 |
| LicMen C | PIII(M3) | 112 | 104 | 92.9 | 86.4 | 96.9 | 82 | 73.2 | 64.0 | 81.1 | 2.576 | 1.871 | 3.546 |
| | PIII(M10) | 110 | 81 | 73.6 | 64.4 | 81.6 | 34 | 30.9 | 22.4 | 40.4 | 0.471 | 0.360 | 0.617 |

N = number of subjects with available results

n (%) = number (percentage) of subjects with anti-PRP antibody concentrations within the specified range

PIII(M3) = post-Dose 3 blood sample at Month 3

PIII(M10) = pre-booster blood sample at Month 10

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

Secondary Outcome Variable (s):

Persistence: seropositivity rates 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 ($\mu\text{g/mL}$) | | |
|-------------|-----------|-----|---------------------------|------|--------|------|-------------------------|------|--------|------|--------------------------|--------|-------|
| | | | n | % | 95% CI | | n | % | 95% CI | | Value | 95% CI | |
| | | | | | LL | UL | | | LL | UL | | LL | UL |
| HibMen C | PIII(M3) | 348 | 347 | 99.7 | 98.4 | 100 | 344 | 98.9 | 97.1 | 99.7 | 9.06 | 8.41 | 9.76 |
| | PIII(M10) | 348 | 294 | 84.5 | 80.2 | 88.1 | 43 | 12.4 | 9.1 | 16.3 | 0.76 | 0.69 | 0.85 |
| LicMen C | PIII(M3) | 109 | 109 | 100 | 96.7 | 100 | 109 | 100 | 96.7 | 100 | 12.92 | 11.43 | 14.59 |
| | PIII(M10) | 110 | 98 | 89.1 | 81.7 | 94.2 | 25 | 22.7 | 15.3 | 31.7 | 0.97 | 0.80 | 1.18 |

N = number of subjects with available results

n (%) = number (percentage) of subjects with anti-PSC antibody concentrations within the specified range

PIII(M3) = post-Dose 3 blood sample at Month 3

PIII(M10) = pre-booster blood sample at Month 10

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

Secondary Outcome Variable (s):

Immune response: seropositivity rates and GMCs for anti-PSC antibodies, pre- and post-booster vaccination (Booster ATP cohort for immunogenicity)

| Group | Timing | N | ≥ 0.3 µg/mL | | | | ≥ 2 µg/mL | | | | GMC (µg/mL) | | |
|----------|------------|-----|-------------|------|--------|------|-----------|------|--------|------|-------------|--------|------|
| | | | n | % | 95% CI | | n | % | 95% CI | | Value | 95% CI | |
| | | | | | LL | UL | | | LL | UL | | LL | UL |
| HibMen C | PIII(M10) | 342 | 288 | 84.2 | 79.9 | 87.9 | 41 | 12.0 | 8.7 | 15.9 | 0.76 | 0.69 | 0.84 |
| | PIV(M11.5) | 349 | 349 | 100 | 98.9 | 100 | 317 | 90.8 | 87.3 | 93.6 | 7.43 | 6.73 | 8.19 |
| LicMen C | PIII(M10) | 110 | 98 | 89.1 | 81.7 | 94.2 | 25 | 22.7 | 15.3 | 31.7 | 0.97 | 0.80 | 1.18 |
| | PIV(M11.5) | 115 | 115 | 100 | 96.8 | 100 | 88 | 76.5 | 67.7 | 83.9 | 3.67 | 3.14 | 4.29 |
| Pooled | PIII(M10) | 452 | 386 | 85.4 | 81.8 | 88.5 | 66 | 14.6 | 11.5 | 18.2 | 0.81 | 0.74 | 0.88 |
| | PIV(M11.5) | 464 | 464 | 100 | 99.2 | 100 | 405 | 87.3 | 83.9 | 90.2 | 6.24 | 5.71 | 6.81 |

N = number of subjects with available results

n (%) = number (percentage) of subjects with anti-PSC antibody concentrations within the specified range

PIII(M10) = pre-booster blood sample at Month 10

PIV(M11.5) = post-booster blood sample at Month 11.5

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

Secondary Outcome Variable (s):

Immune response: seroconversion rates and GMCs for anti-measles antibodies, pre- and post-booster vaccination (on initially seronegative subjects) (Booster ATP cohort for immunogenicity)

| Group | Timing | N | ≥ 150 mIU/mL | | | | GMC (mIU/mL) | | | |
|----------|------------|-----|--------------|------|--------|------|--------------|--------|--------|--|
| | | | n | % | 95% CI | | Value | 95% CI | | |
| | | | | | LL | UL | | LL | UL | |
| HibMen C | PIII(M10) | 339 | 0 | 0.0 | 0.0 | 1.1 | 75.0 | 75.0 | 75.0 | |
| | PIV(M11.5) | 338 | 334 | 98.8 | 97.0 | 99.7 | 2616.1 | 2386.5 | 2867.8 | |
| LicMen C | PIII(M10) | 109 | 0 | 0.0 | 0.0 | 3.3 | 75.0 | 75.0 | 75.0 | |
| | PIV(M11.5) | 108 | 104 | 96.3 | 90.8 | 99.0 | 2460.8 | 2019.4 | 2998.6 | |
| Pooled | PIII(M10) | 448 | 0 | 0.0 | 0.0 | 0.8 | 75.0 | 75.0 | 75.0 | |
| | PIV(M11.5) | 446 | 438 | 98.2 | 96.5 | 99.2 | 2577.6 | 2369.6 | 2803.8 | |

N = number of subjects with available results

n (%) = number (percentage) of subjects with anti-measles antibody concentrations within the specified range

PIII(M10) = pre-booster blood sample at Month 10

PIV(M11.5) = post-booster blood sample at Month 11.5

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

Secondary Outcome Variable (s):

Immune response: seroconversion rates and GMCs for anti-mumps antibodies, pre- and post-booster vaccination (on initially seronegative subjects) (Booster ATP cohort for immunogenicity)

| Group | Timing | N | ≥ 231 U/mL | | | | GMC (U/mL) | | | |
|---------|------------|-----|------------|----------|--------|------|------------|--------|--------|--|
| | | | N | % | 95% CI | | Value | 95% CI | | |
| | | | | | LL | UL | | LL | UL | |
| HibMenC | PIII(M10) | 341 | 0 | 0.0 | 0.0 | 1.1 | 115.5 | 115.5 | 115.5 | |
| | PIV(M11.5) | 327 | 31 0 | 94. 8 | 91.8 | 96.9 | 983.4 | 895.7 | 1079.7 | |
| LicMenC | PIII(M10) | 110 | 0 | 0.0 | 0.0 | 3.3 | 115.5 | 115.5 | 115.5 | |
| | PIV(M11.5) | 107 | 10 5 | 98. 1 | 93.4 | 99.8 | 1090.0 | 939.1 | 1265.1 | |
| Pooled | PIII(M10) | 451 | 0 | 0.0 | 0.0 | 0.8 | 115.5 | 115.5 | 115.5 | |
| | PIV(M11.5) | 434 | 41 5 | 95. 6 | 93.2 | 97.3 | 1008.6 | 931.8 | 1091.8 | |

N = number of subjects with available results
n (%) = number (percentage) of subjects with anti-mumps antibody concentrations within the specified range

PIII(M10) = pre-booster blood sample at Month 10

PIV(M11.5) = post-booster blood sample at Month 11.5

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

Secondary Outcome Variable (s):

Immune response: seroconversion rates and GMCs for anti-rubella antibodies, pre- and post-booster vaccination (on initially seronegative subjects) (Booster ATP cohort for immunogenicity)

| Group | Timing | N | ≥ 4 IU/mL | | | | GMC (IU/mL) | | | |
|---------|------------|-----|-----------|------|--------|------|-------------|--------|------|--|
| | | | n | % | 95% CI | | Value | 95% CI | | |
| | | | | | LL | UL | | LL | UL | |
| HibMenC | PIII(M10) | 338 | 0 | 0.0 | 0.0 | 1.1 | 2.0 | 2.0 | 2.0 | |
| | PIV(M11.5) | 338 | 336 | 99.4 | 97.9 | 99.9 | 62.4 | 57.2 | 68.1 | |
| LicMenC | PIII(M10) | 108 | 0 | 0.0 | 0.0 | 3.4 | 2.0 | 2.0 | 2.0 | |
| | PIV(M11.5) | 107 | 107 | 100 | 96.6 | 100 | 70.5 | 59.7 | 83.2 | |
| Pooled | PIII(M10) | 446 | 0 | 0.0 | 0.0 | 0.8 | 2.0 | 2.0 | 2.0 | |
| | PIV(M11.5) | 445 | 443 | 99.6 | 98.4 | 99.9 | 64.2 | 59.5 | 69.4 | |

N = number of subjects with available results

n (%) = number (percentage) of subjects with anti-rubella antibody concentrations within the specified range

PIII(M10) = pre-booster blood sample at Month 10

PIV(M11.5) = post-booster blood sample at Month 11.5

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

Secondary Outcome Variable (s):

Persistence: seroprotection rates and GMCs for anti-diphtheria antibodies (ATP cohort for antibody persistence)

| Group | Timing | N | ≥ 0.1 IU/mL | | | | GMC (IU/mL) | | | |
|---------|-----------|-----|-------------|------|--------|------|-------------|--------|------|--|
| | | | N | % | 95% CI | | Value | 95% CI | | |
| | | | | | LL | UL | | LL | UL | |
| HibMenC | PIII(M3) | 349 | 343 | 98.3 | 96.3 | 99.4 | 0.83 | 0.74 | 0.92 | |
| | PIII(M10) | 347 | 157 | 45.2 | 39.9 | 50.6 | 0.10 | 0.09 | 0.11 | |
| LicMenC | PIII(M3) | 112 | 112 | 100 | 96.8 | 100 | 1.78 | 1.51 | 2.10 | |
| | PIII(M10) | 110 | 98 | 89.1 | 81.7 | 94.2 | 0.28 | 0.24 | 0.33 | |

N = number of subjects with available results

n (%) = number (percentage) of subjects with anti-diphtheria antibody concentrations within the specified range

PIII(M3) = post-Dose 3 blood sample at Month 3

PIII(M10) = pre-booster blood sample at Month 10

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

Secondary Outcome Variable (s):

Persistence: seroprotection rates and GMCs for anti-tetanus antibodies (ATP cohort for antibody persistence)

| Group | Timing | N | ≥ 0.1 IU/mL | | | | GMC (IU/mL) | | |
|---------|-----------|-----|-------------|------|--------|------|-------------|--------|------|
| | | | n | % | 95% CI | | Value | 95% CI | |
| | | | | | LL | UL | | LL | UL |
| HibMenC | PIII(M3) | 349 | 349 | 100 | 98.9 | 100 | 2.35 | 2.19 | 2.52 |
| | PIII(M10) | 348 | 338 | 97.1 | 94.8 | 98.6 | 0.57 | 0.53 | 0.62 |
| LicMenC | PIII(M3) | 112 | 111 | 99.1 | 95.1 | 100 | 0.88 | 0.75 | 1.04 |
| | PIII(M10) | 110 | 87 | 79.1 | 70.3 | 86.3 | 0.21 | 0.18 | 0.26 |

N = number of subjects with available results

n (%) = number (percentage) of subjects with anti-tetanus antibody concentrations within the specified range

PIII(M3) = post-Dose 3 blood sample at Month 3

PIII(M10) = pre-booster blood sample at Month 10

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

Secondary Outcome Variable (s):

Persistence: seroprotection rates and GMTs for anti-polio 1, anti-polio 2 and anti-polio 3 antibodies (ATP cohort for antibody persistence)

| Antibody | Group | Timing | N | ≥ 8 | | | | GMT | | |
|--------------|---------|-----------|-----|-----|------|--------|------|-------|--------|-------|
| | | | | n | % | 95% CI | | Value | 95% CI | |
| | | | | | | LL | UL | | LL | UL |
| Anti-polio 1 | HibMenC | PIII(M3) | 313 | 312 | 99.7 | 98.2 | 100 | 185.4 | 163.9 | 209.6 |
| | | PIII(M10) | 322 | 292 | 90.7 | 87.0 | 93.6 | 43.5 | 37.8 | 50.0 |
| | LicMenC | PIII(M3) | 99 | 97 | 98.0 | 92.9 | 99.8 | 100.2 | 79.1 | 126.9 |
| | | PIII(M10) | 103 | 90 | 87.4 | 79.4 | 93.1 | 31.3 | 24.5 | 39.9 |
| Anti-polio 2 | HibMenC | PIII(M3) | 307 | 303 | 98.7 | 96.7 | 99.6 | 117.5 | 101.4 | 136.1 |
| | | PIII(M10) | 317 | 298 | 94.0 | 90.8 | 96.4 | 39.5 | 34.8 | 44.9 |
| | LicMenC | PIII(M3) | 98 | 96 | 98.0 | 92.8 | 99.8 | 101.1 | 81.1 | 126.1 |
| | | PIII(M10) | 101 | 90 | 89.1 | 81.3 | 94.4 | 35.0 | 27.6 | 44.5 |
| Anti-polio 3 | HibMenC | PIII(M3) | 292 | 289 | 99.0 | 97.0 | 99.8 | 440.4 | 381.2 | 508.8 |
| | | PIII(M10) | 319 | 305 | 95.6 | 92.7 | 97.6 | 83.7 | 73.0 | 95.9 |
| | LicMenC | PIII(M3) | 95 | 95 | 100 | 96.2 | 100 | 222.9 | 175.7 | 282.8 |
| | | PIII(M10) | 101 | 90 | 89.1 | 81.3 | 94.4 | 49.0 | 37.4 | 64.1 |

N = number of subjects with available results

n (%) = number (percentage) of subjects with anti-polio antibody titers within the specified range

PIII(M3) = post-Dose 3 blood sample at Month 3

PIII(M10) = pre-booster blood sample at Month 10

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

Secondary Outcome Variable (s):

Persistence: seropositivity rates and GMCs for anti-PT, anti-FHA and anti-PRN antibodies (ATP cohort for antibody persistence)

| 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 | PIII(M3) | 349 | 34 8 | 99. 7 | 98. 4 | 100 | 44.0 | 41.4 | 46.8 |
| | | PIII(M10) | 346 | 23 3 | 67. 3 | 62. 1 | 72.3 | 7.1 | 6.5 | 7.8 |
| | LicMenC | PIII(M3) | 112 | 11 2 | 10 0 | 96. 8 | 100 | 35.3 | 32.0 | 38.8 |
| | | PIII(M10) | 110 | 67 | 60. 9 | 51. 1 | 70.1 | 5.6 | 4.9 | 6.5 |
| Anti-FHA | HibMenC | PIII(M3) | 349 | 34 8 | 99. 7 | 98. 4 | 100 | 151.5 | 140.9 | 162.9 |
| | | PIII(M10) | 345 | 33 9 | 98. 3 | 96. 3 | 99.4 | 33.7 | 30.5 | 37.4 |
| | LicMenC | PIII(M3) | 112 | 11 2 | 10 0 | 96. 8 | 100 | 116.8 | 103.3 | 131.9 |
| | | PIII(M10) | 110 | 10 8 | 98. 2 | 93. 6 | 99.8 | 25.2 | 21.8 | 29.0 |
| Anti-PRN | HibMenC | PIII(M3) | 349 | 34 5 | 98. 9 | 97. 1 | 99.7 | 79.4 | 71.2 | 88.6 |
| | | PIII(M10) | 348 | 26 8 | 77. 0 | 72. 2 | 81.3 | 11.7 | 10.4 | 13.1 |
| | LicMenC | PIII(M3) | 112 | 10 9 | 97. 3 | 92. 4 | 99.4 | 37.1 | 30.3 | 45.3 |
| | | PIII(M10) | 109 | 70 | 64. 2 | 54. 5 | 73.2 | 7.1 | 5.9 | 8.6 |

N = number of subjects with available results

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

PIII(M3) = post-Dose 3 blood sample at Month 3

PIII(M10) = pre-booster blood sample at Month 10

95% CI = 95% confidence interval; LL = lower limit; UL = upper limit

Secondary Outcome Variable (s):

Number and percentage of subjects with solicited local symptoms during the 4-day (Day 0-3) follow-up period (Booster Total Vaccinated cohort)

| Symptom | Intensity | HibMenC Group | | | | | LicMenC Group | | | | | Pooled Group | | | | |
|-----------------|------------------|----------------------|----------|----------|---------------|-----------|----------------------|----------|----------|---------------|-----------|---------------------|----------|----------|---------------|-----------|
| | | N | n | % | 95% CI | | N | n | % | 95% CI | | N | n | % | 95% CI | |
| | | | | | LL | UL | | | | LL | UL | | | | LL | UL |
| Pain | Any | 359 | 69 | 19.2 | 15.3 | 23.7 | 117 | 22 | 18.8 | 12.2 | 27.1 | 476 | 91 | 19.1 | 15.7 | 22.9 |
| | Grade 3 | 359 | 2 | 0.6 | 0.1 | 2.0 | 117 | 1 | 0.9 | 0.0 | 4.7 | 476 | 3 | 0.6 | 0.1 | 1.8 |
| Redness | Any | 359 | 126 | 35.1 | 30.2 | 40.3 | 117 | 39 | 33.3 | 24.9 | 42.6 | 476 | 165 | 34.7 | 30.4 | 39.1 |
| | > 30 mm | 359 | 3 | 0.8 | 0.2 | 2.4 | 117 | 1 | 0.9 | 0.0 | 4.7 | 476 | 4 | 0.8 | 0.2 | 2.1 |
| Swelling | Any | 359 | 71 | 19.8 | 15.8 | 24.3 | 117 | 13 | 11.1 | 6.1 | 18.3 | 476 | 84 | 17.6 | 14.3 | 21.4 |
| | > 30 mm | 359 | 3 | 0.8 | 0.2 | 2.4 | 117 | 0 | 0.0 | 0.0 | 3.1 | 476 | 3 | 0.6 | 0.1 | 1.8 |

N = number of subjects with a symptom sheet completed

n (%) = number (percentage) of subjects for whom a specific symptom was reported at least once

Any = incidence of a particular symptom regardless of intensity

Grade 3 Pain = cried when limb was moved / spontaneously painful

95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit

Secondary Outcome Variable (s):

Number and percentage of subjects with solicited general symptoms during the 4-day (Day 0-3)

follow-up period (Booster Total Vaccinated cohort)

| Symptom | Intensity/ relationship | HibMenC Group | | | | | LicMenC Group | | | | | Pooled Group | | | | |
|------------------|----------------------------|---------------|-----|------|--------|------|---------------|----|------|--------|------|--------------|-----|------|--------|------|
| | | N | n | % | 95% CI | | N | n | % | 95% CI | | N | n | % | 95% CI | |
| | | | | | LL | UL | | | | LL | UL | | | | LL | UL |
| Drowsiness | Any | 359 | 83 | 23.1 | 18.9 | 27.8 | 117 | 26 | 22.2 | 15.1 | 30.8 | 476 | 109 | 22.9 | 19.2 | 26.9 |
| | Grade 3 | 359 | 3 | 0.8 | 0.2 | 2.4 | 117 | 0 | 0.0 | 0.0 | 3.1 | 476 | 3 | 0.6 | 0.1 | 1.8 |
| | Related | 359 | 78 | 21.7 | 17.6 | 26.4 | 117 | 25 | 21.4 | 14.3 | 29.9 | 476 | 103 | 21.6 | 18.0 | 25.6 |
| Irritability | Any | 359 | 144 | 40.1 | 35.0 | 45.4 | 117 | 42 | 35.9 | 27.2 | 45.3 | 476 | 186 | 39.1 | 34.7 | 43.6 |
| | Grade 3 | 359 | 3 | 0.8 | 0.2 | 2.4 | 117 | 2 | 1.7 | 0.2 | 6.0 | 476 | 5 | 1.1 | 0.3 | 2.4 |
| | Related | 359 | 134 | 37.3 | 32.3 | 42.6 | 117 | 40 | 34.2 | 25.7 | 43.5 | 476 | 174 | 36.6 | 32.2 | 41.1 |
| Loss of appetite | Any | 359 | 91 | 25.3 | 20.9 | 30.2 | 117 | 27 | 23.1 | 15.8 | 31.8 | 476 | 118 | 24.8 | 21.0 | 28.9 |
| | Grade 3 | 359 | 1 | 0.3 | 0.0 | 1.5 | 117 | 0 | 0.0 | 0.0 | 3.1 | 476 | 1 | 0.2 | 0.0 | 1.2 |
| | Related | 359 | 86 | 24.0 | 19.6 | 28.7 | 117 | 26 | 22.2 | 15.1 | 30.8 | 476 | 112 | 23.5 | 19.8 | 27.6 |
| Fever (rectally) | ≥ 38.0 °C | 359 | 55 | 15.3 | 11.8 | 19.5 | 117 | 14 | 12.0 | 6.7 | 19.3 | 476 | 69 | 14.5 | 11.5 | 18.0 |
| | > 40.0 °C | 359 | 2 | 0.6 | 0.1 | 2.0 | 117 | 0 | 0.0 | 0.0 | 3.1 | 476 | 2 | 0.4 | 0.1 | 1.5 |
| | Related | 359 | 40 | 11.1 | 8.1 | 14.9 | 117 | 11 | 9.4 | 4.8 | 16.2 | 476 | 51 | 10.7 | 8.1 | 13.8 |

N = number of subjects with a symptom sheet completed

n (%) = number (percentage) of subjects for whom a specific symptom was reported at least once

Any = incidence of a particular symptom regardless of intensity and relationship to vaccination

Related = symptom considered by the investigator to have a causal relationship to study vaccination

Grade 3 Drowsiness = Drowsiness that prevented normal activity

Grade 3 Irritability/Fussiness = Crying that could not be comforted/prevented normal activity

Grade 3 Loss of appetite = Not eating at all

95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit

Secondary Outcome Variable (s):

Percentage of subjects with MMR specific solicited symptoms reported during the 43-day (Day 0-42) post-vaccination period (Booster Total Vaccinated cohort)

| Symptom | Intensity/ relationship | HibMenC Group | | | | | LicMenC Group | | | | | Pooled Group | | | | |
|---|----------------------------|---------------|----|------|--------|------|---------------|----|------|--------|------|--------------|----|------|--------|------|
| | | N | n | % | 95% CI | | N | n | % | 95% CI | | N | n | % | 95% CI | |
| | | | | | LL | UL | | | | LL | UL | | | | LL | UL |
| Suspected signs of meningism/ including febrile convulsions | Any | 359 | 1 | 0.3 | 0.0 | 1.5 | 117 | 0 | 0.0 | 0.0 | 3.1 | 476 | 1 | 0.2 | 0.0 | 1.2 |
| | Grade 3 | 359 | 1 | 0.3 | 0.0 | 1.5 | 117 | 0 | 0.0 | 0.0 | 3.1 | 476 | 1 | 0.2 | 0.0 | 1.2 |
| | Related | 359 | 1 | 0.3 | 0.0 | 1.5 | 117 | 0 | 0.0 | 0.0 | 3.1 | 476 | 1 | 0.2 | 0.0 | 1.2 |
| Parotid/ salivary gland swelling | Any | 359 | 3 | 0.8 | 0.2 | 2.4 | 117 | 4 | 3.4 | 0.9 | 8.5 | 476 | 7 | 1.5 | 0.6 | 3.0 |
| | Grade 3 | 359 | 1 | 0.3 | 0.0 | 1.5 | 117 | 0 | 0.0 | 0.0 | 3.1 | 476 | 1 | 0.2 | 0.0 | 1.2 |
| | Related | 359 | 3 | 0.8 | 0.2 | 2.4 | 117 | 3 | 2.6 | 0.5 | 7.3 | 476 | 6 | 1.3 | 0.5 | 2.7 |
| Rash/ exanthem | Any | 359 | 62 | 17.3 | 13.5 | 21.6 | 117 | 21 | 17.9 | 11.5 | 26.1 | 476 | 83 | 17.4 | 14.1 | 21.2 |
| | Grade 3 | 359 | 15 | 4.2 | 2.4 | 6.8 | 117 | 7 | 6.0 | 2.4 | 11.9 | 476 | 22 | 4.6 | 2.9 | 6.9 |
| | Related | 359 | 41 | 11.4 | 8.3 | 15.2 | 117 | 13 | 11.1 | 6.1 | 18.3 | 476 | 54 | 11.3 | 8.6 | 14.5 |

| | | | | | | | | | | | | | | | | |
|-------------------------|-----------|-----|-----|------|------|------|-----|----|------|------|------|-----|----|------|------|------|
| Fever (rectally) | ≥ 38.0 °C | 359 | 218 | 60.7 | 55.5 | 65.8 | 117 | 64 | 54.7 | 45.2 | 63.9 | 476 | 28 | 59.2 | 54.7 | 63.7 |
| | > 40.0 °C | 359 | 17 | 4.7 | 2.8 | 7.5 | 117 | 6 | 5.1 | 1.9 | 10.8 | 476 | 23 | 4.8 | 3.1 | 7.2 |
| | Related | 359 | 143 | 39.8 | 34.7 | 45.1 | 117 | 41 | 35.0 | 26.5 | 44.4 | 476 | 18 | 38.4 | 34.7 | 43.2 |

N = number of subjects with a symptom sheet completed
n (%) = number (percentage) of subjects for whom a specific symptom was reported at least once
Any = incidence of a particular symptom regardless of intensity and relationship to vaccination
Grade 3 Suspected signs of meningism / including febrile convulsions = symptoms which prevented normal, everyday activities.
Grade 3 Parotid / Salivary gland swelling = swelling, with accompanying general symptoms
Grade 3 Rash/exanthem ≥ 150 lesions
Related = symptoms considered by the investigator to have a causal relationship to study vaccination
95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit

Safety Results: Number (%) of subjects with unsolicited adverse events (AEs) (Booster Total Vaccinated cohort)

| Most Frequent Adverse Events - On-Therapy (occurring within Day 0-30 following vaccination) | HibMenC Group N = 359 | LicMenC Group N = 117 | Pooled Group N = 476 |
|--|----------------------------------|----------------------------------|---------------------------------|
| Subjects with any AE(s), n (%) | 169 (47.1) | 56 (47.9) | 225 (47.3) |
| Teething | 57 (15.9) | 21 (17.9) | 78 (16.4) |
| Rhinitis | 32 (8.9) | 8 (6.8) | 40 (8.4) |
| Gastroenteritis | 27 (7.5) | 3 (2.6) | 30 (6.3) |
| Diarrhea | 17 (4.7) | 5 (4.3) | 22 (4.6) |
| Vomiting | 15 (4.2) | 7 (6.0) | 22 (4.6) |
| Pharyngitis | 12 (3.3) | 6 (5.1) | 18 (3.8) |
| Upper respiratory tract infection | 12 (3.3) | 2 (1.7) | 14 (2.9) |
| Bronchitis | 7 (1.9) | 4 (3.4) | 11 (2.3) |
| Conjunctivitis | 7 (1.9) | 4 (3.4) | 11 (2.3) |
| Injection site bruising | 4 (1.1) | 4 (3.4) | 8 (1.7) |
| Irritability | 5 (1.4) | 3 (2.6) | 8 (1.7) |
| Cough | 5 (1.4) | 2 (1.7) | 7 (1.5) |
| Ear infection | 2 (0.6) | 4 (3.4) | 6 (1.3) |
| Nasopharyngitis | 5 (1.4) | 1 (0.9) | 6 (1.3) |
| Viral infection | 5 (1.4) | 0 (0.0) | 5 (1.1) |

Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) from the end of the primary phase until the start of the booster vaccination (Booster Total Vaccinated cohort)

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 | Pooled Group N = 476 |
|---|----------------------------------|----------------------------------|---------------------------------|
| Subjects with any SAE(s), n (%) [n related] | 28 (7.8) [0] | 5 (4.3) [0] | 33 (6.9) [0] |
| Gastroenteritis | 9 (2.5) [0] | 1 (0.9) [0] | 10 (2.1) [0] |
| Pneumonia | 2 (0.6) [0] | 1 (0.9) [0] | 3 (0.6) [0] |
| Wheezing | 3 (0.8) [0] | 0 (0.0) [0] | 3 (0.6) [0] |
| Bronchiolitis | 2 (0.6) [0] | 0 (0.0) [0] | 2 (0.4) [0] |
| Bronchopneumonia | 1 (0.3) [0] | 1 (0.9) [0] | 2 (0.4) [0] |
| Diarrhea | 2 (0.6) [0] | 0 (0.0) [0] | 2 (0.4) [0] |
| Enterocolitis | 2 (0.6) [0] | 0 (0.0) [0] | 2 (0.4) [0] |
| Febrile convulsion | 1 (0.3) [0] | 1 (0.9) [0] | 2 (0.4) [0] |

| | | | |
|--|----------------------------------|----------------------------------|---------------------------------|
| Laryngitis | 1 (0.3) [0] | 1 (0.9) [0] | 2 (0.4) [0] |
| Upper respiratory tract infection | 2 (0.6) [0] | 0 (0.0) [0] | 2 (0.4) [0] |
| Bronchitis | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Bronchitis chronic | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Cellulitis | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Craniosynostosis | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Croup infectious | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Deafness | 0 (0.0) [0] | 1 (0.9) [0] | 1 (0.2) [0] |
| Femur fracture | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Food allergy | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Gastroenteritis rotavirus | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Iron deficiency anemia | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Laryngotracheo bronchitis | 0 (0.0) [0] | 1 (0.9) [0] | 1 (0.2) [0] |
| Lower respiratory tract infection | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Nasopharyngitis | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Pharyngitis | 0 (0.0) [0] | 1 (0.9) [0] | 1 (0.2) [0] |
| Pyelonephritis | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Thermal burn | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Urinary tract infection | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Vomiting | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Fatal SAEs | HibMenC Group N = 359 | LicMenC Group N = 117 | Pooled Group N = 476 |
| Subjects with fatal SAE(s), n (%) [n related] | 0 (0.0) [0] | 0 (0.0) [0] | 0 (0.0) [0] |
| Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) after booster vaccination (Booster Total Vaccinated cohort) | | | |
| 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 | Pooled Group N = 476 |
| Subjects with any SAE(s), n (%) [n related] | 8 (2.2) [1] | 4 (3.4) [0] | 12 (2.5) [1] |
| Gastroenteritis | 2 (0.6) [0] | 2 (1.7) [0] | 4 (0.8) [0] |
| Pneumonia | 2 (0.6) [0] | 1 (0.9) [0] | 3 (0.6) [0] |
| Gastroenteritis rotavirus | 2 (0.6) [0] | 0 (0.0) [0] | 2 (0.4) [0] |
| Anemia | 0 (0.0) [0] | 1 (0.9) [0] | 1 (0.2) [0] |
| Asthma | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Hemorrhagic diathesis | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Otitis media acute | 1 (0.3) [0] | 0 (0.0) [0] | 1 (0.2) [0] |
| Pyrexia | 1 (0.3) [1] | 0 (0.0) [0] | 1 (0.2) [1] |
| Viral rash | 0 (0.0) [0] | 1 (0.9) [0] | 1 (0.2) [0] |
| Fatal SAEs | HibMenC Group N = 359 | LicMenC Group N = 117 | Pooled Group N = 476 |
| Subjects with fatal SAE(s), n (%) [n related] | 0 (0.0) [0] | 0 (0.0) [0] | 0 (0.0) [0] |

Conclusion: At 42 days after the booster vaccination, 97.7% and 86.0% of the subjects from HibMenC Group and LicMenC Group, respectively had rSBA-MenC antibody titers $\geq 1:128$. At the same time point, all subjects had anti-PRP antibody concentrations $\geq 1 \mu\text{g/mL}$. Across groups, redness and irritability were the most frequently reported solicited local and general symptoms, respectively. During the 43-day follow-up period for MMR symptoms, fever was the most frequently reported symptom. Unsolicited AEs were reported for 169 (47.1%) and 56 (47.9%) of the subjects from HibMenC Group and LicMenC Group, respectively. Since the end of the primary phase and before the start of the booster phase of the study, SAEs were reported for 28 (7.8%) and 5 (4.3%) of the subjects from HibMenC Group and LicMenC Group, respectively. These SAEs were considered by the investigators not to be related to the study vaccination. From the start of the booster phase of the study, SAEs were reported for 8 (2.2%) and 4 (3.4%) of the subjects from HibMenC Group and LicMenC Group, respectively; 1 SAE in the HibMenC Group was considered by the investigator to be related to the study vaccination (fever [$\leq 38.5^\circ\text{C}$ rectally] with no signs of infection). No fatal SAEs were reported during the whole course of the study.

Publications: Snape et al (2007) Immunogenicity of a combined Haemophilus influenzae type b and Neisseria meningitidis serogroup C-tetanus toxoid booster vaccine at age 12 months. Poster presented at ESPID 2007

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