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.

Study No.: 112993 (SPNG-006 BST:001)

Title: A study to evaluate safety & immunogenicity of a booster dose of two formulations of GSK Biologicals' pneumococcal protein candidate vaccine in healthy young adults.
GSK2189242A (PlPh): GSK (GlaxoSmithKline) Biologicals' pneumococcal protein candidate vaccine.
GSK2189242A Formulation 1 (PlPh 1)*: GSK Biologicals' GSK2189242A candidate pneumococcal vaccine, formulation 1.
GSK2189242A Formulation 2 (PlPh 2)*: GSK Biologicals' GSK2189242A candidate pneumococcal vaccine, formulation 2.
**Note: The PlPh 1 and PlPh 2 vaccines in this study correspond, respectively, to the Formulations 3 and 4 of the PV vaccine as per the 111651 CTRS for the SPNG-001 (111651) primary vaccination study.*

Rationale: The aim of this study was to evaluate the safety and immunogenicity of the PlPh 1 and PlPh 2 vaccines when given as a booster dose to a healthy young adult population previously vaccinated with the same vaccines in the primary vaccination study SPNG-001 (111651). In addition, the immunogenicity of the PlPh 1 and PlPh 2 vaccines and the persistence of antibodies against the antigens contained in these two vaccines were evaluated.
For results of the SPNG-001 (111651) primary vaccination study, please refer to the 111651 CTRS.

Phase: II

Study Period: 18 May 2009 to 05 August 2009

Study Design: Double-blind, randomized and controlled study with 2 parallel groups (1:1).

Centers: 1 center in Belgium.

Indication: Booster immunization against *Streptococcus pneumoniae* (*S. pneumoniae*) of healthy adults aged between 18 and 41 years old.

Treatment: The study groups were as follows:

- PlPh 1 Group*: Subjects previously primed with the PlPh 1 vaccine during the 111651 study, received a booster dose of the PlPh 1 vaccine at Day 0.
- PlPh 2 Group*: Subjects previously primed with the PlPh 2 vaccine during the 111651 study received a booster dose of the PlPh 2 vaccine at Day 0.

Both vaccines were administered via intramuscular injection into the deltoid of the non-dominant arm.
**Note: The PlPh 1 and PlPh2 groups in this study correspond, respectively, to the PV 3 and 4 groups during the SPNG-001 (111651) vaccination primary study.*

Objectives:

- To assess the safety of a booster dose of the PlPh 1 and PlPh 2 vaccines when administered intramuscularly in healthy adults, in terms of vaccine-related and grade 3 solicited, unsolicited adverse events (AEs) and haematological or biochemical abnormalities and vaccine-related serious adverse events (SAEs).

Primary Outcome/Efficacy Variable:
*Safety:*

- Occurrence of any vaccine-related and grade 3 solicited local and general AEs during the 7-day (follow-up period (i.e. day of vaccination and 6 subsequent days) after vaccination.
- Occurrence of any vaccine-related and grade 3 unsolicited AEs during the 31-day follow-up period (i.e. day of vaccination and 30 subsequent days) after vaccination.
- Occurrence of any vaccine-related SAEs occurring during the entire study period (from Day 0 to Day 30).
- Occurrence of any grade 3 haematological or biochemical abnormalities, at 1 and 7* days after vaccination.

**Note: Blood samples were collected at Days 1 and 6.*

Secondary Outcome/Efficacy Variables:
*Immunogenicity:*
Evaluation of the immune responses to components of the PlPh 1 and PlPh 2 vaccines, prior to the booster vaccination and one month post-booster vaccination.

- Concentrations of antibodies against pneumococcal pneumolysin toxoid (dPly) and histidine triad protein D (PhtD) proteins.

*Safety:*

- Occurrence of any solicited local and general AEs during the 7-day follow-up period (Days 0-6) after vaccination.
- Occurrence of any unsolicited AEs during the 31-day follow-up period (Days 0-30) after vaccination.
- Occurrence of any SAEs occurring during the entire study period (from Days 0-30).
- Occurrence of any haematological or biochemical abnormalities at 1 and 7* days after vaccination.

*Blood samples were collected at Day 1 and at Day 6.

Statistical Methods:

The analyses were performed on the Total Vaccinated cohort and the According-To-Protocol (ATP) cohort for immunogenicity:

- The Total Vaccinated cohort included all subjects with study vaccine administration documented.
- The ATP cohort for immunogenicity included all evaluable subjects (i.e. those meeting all eligibility criteria, complying with the procedures defined in the protocol, with no elimination criteria during the study) for whom post results were available for at least one assay.

*Analysis of Immunogenicity*

The analysis of immunogenicity was performed on the ATP cohort for immunogenicity.

At each time point that a blood sample result was available, for each antibody assessed and for each treatment group, geometric mean antibody concentrations/titers (GMCs/GMTs) and seropositivity* rates were calculated with their 95% confidence interval (CI)

*Analysis of Safety*

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

The percentage of subjects with each individual solicited local and general symptom within the 7-day (Days 0-6) follow-up period following booster vaccination was summarized with its exact 95% CI for each group. The same tabulation was performed for grade 3 symptoms and for general symptoms assessed by the investigator as causally related to vaccination. All solicited local symptoms were assessed as causally related to the study vaccination. The percentage of subjects with unsolicited AEs within the 31-day (Days 0-30) follow-up period following booster vaccination were tabulated according to the Medical Dictionary for Regulatory Activities (MedDRA) preferred term for each group. The same tabulation was performed for grade 3 AEs and for AEs assessed by the investigator as having a causal relationship to vaccination. The occurrence of SAEs and that of SAEs assessed by the investigator as causally related to study vaccination reported during the entire study period (from Day 0 up to the study end at Day 30) were tabulated according to MedDRA preferred terms. For each haematology and biochemistry parameter, the grading was summarized per study group, at Day 1 and at Day 6 after booster vaccination.

*A seropositive subject was defined as a subject whose antibody concentration/titer was greater than or equal to the pre-specified assay cut-off value (titer ≥ 6 for anti-pneumolysin haemolysis (Hem-dPly), concentration ≥ 599 LU/mL for anti-dPly, and concentration ≥ 391 LU/mL for anti-PhtD).

Study Population: Male and female subjects aged between 18 and 41 years old at the time of vaccination, previously primed during the primary vaccination study SPNG-001 (111651) with either the PIPh 1 or PIPh 2 vaccine, were enrolled in this booster study. Subjects documented with bacterial pneumonia or invasive pneumococcal disease within the period between the end of the 111651 primary study and this booster study were excluded. Female subjects were to be of non-childbearing potential, or if the subject was of childbearing potential, she had to be abstinent or had to practice adequate contraception for 30 days prior to vaccination and agreed to continue such precautions for 2 months after completion of the vaccination course. Written informed consent obtained from the subjects prior to any study procedure.

| Number of subjects | PIPh 1 Group | PIPh 2 Group |
|---|---|---|
| Planned, N | 24 | 24 |
| Randomized, N (Total Vaccinated cohort) | 22 | 21 |
| Completed, n (%) | 22 (100) | 21 (100) |
| Total Number Subjects Withdrawn, n (%) | 0 (0.0) | 0 (0.0) |
| 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 (%) | 0 (0.0) | 0 (0.0) |
| **Demographics** | **PIPh 1 Group** | **PIPh 2 Group** |
| N (Total Vaccinated cohort) | 22 | 21 |
| Females:Males | 15:7 | 12:9 |
| Mean Age, years (SD) | 26.7 (4.80) | 23.9 (4.11) |
| White - Caucasian / European heritage, n (%) | 22 (100) | 21 (100) |

Primary Efficacy Results: Number (%) of subjects reporting solicited local symptoms during the 7-day (Days 0-6) post-booster vaccination period (Total Vaccinated cohort)

| Symptom | Intensity | PIPh 1 Group | | | | | PIPh 2 Group | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 95 % CI | | | | | 95 % CI | |
| | | N | n | % | LL | UL | N | n | % | LL | UL |
| Pain | Any | 22 | 19 | 86.4 | 65.1 | 97.1 | 21 | 21 | 100 | 83.9 | 100 |
| | Grade 3* | 22 | 0 | 0.0 | 0.0 | 15.4 | 21 | 1 | 4.8 | 0.1 | 23.8 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Redness | Any | 22 | 4 | 18.2 | 5.2 | 40.3 | 21 | 9 | 42.9 | 21.8 | 66.0 |
| | > 50.0 mm* | 22 | 0 | 0.0 | 0.0 | 15.4 | 21 | 1 | 4.8 | 0.1 | 23.8 |
| Swelling | Any | 22 | 2 | 9.1 | 1.1 | 29.2 | 21 | 8 | 38.1 | 18.1 | 61.6 |
| | > 50.0 mm* | 22 | 1 | 4.5 | 0.1 | 22.8 | 21 | 0 | 0.0 | 0.0 | 16.1 |

N = number of subjects with the documented dose
n/% = number/percentage of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit
Any = occurrence of any local symptom regardless of intensity grade
Grade 3 pain = significant pain at rest, pain that prevented normal everyday activity
*Primary outcome variable.

Primary Efficacy Results: Number (%) of subjects reporting solicited general symptoms during the 7-day (Days 0-6) post-booster vaccination period (Total Vaccinated cohort)

| | | PlPh 1 Group | | | | | PlPh 2 Group | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 95 % CI | | | | | 95 % CI | |
| Symptom | Intensity/Relationship | N | n | % | LL | UL | N | n | % | LL | UL |
| Fatigue | Any | 22 | 4 | 18.2 | 5.2 | 40.3 | 21 | 13 | 61.9 | 38.4 | 81.9 |
| | Grade 3* | 22 | 1 | 4.5 | 0.1 | 22.8 | 21 | 0 | 0.0 | 0.0 | 16.1 |
| | Related* | 22 | 3 | 13.6 | 2.9 | 34.9 | 21 | 13 | 61.9 | 38.4 | 81.9 |
| Gastrointestinal symptoms[£] | Any | 22 | 3 | 13.6 | 2.9 | 34.9 | 21 | 1 | 4.8 | 0.1 | 23.8 |
| | Grade 3* | 22 | 0 | 0.0 | 0.0 | 15.4 | 21 | 0 | 0.0 | 0.0 | 16.1 |
| | Related* | 22 | 3 | 13.6 | 2.9 | 34.9 | 21 | 0 | 0.0 | 0.0 | 16.1 |
| Headache | Any | 22 | 5 | 22.7 | 7.8 | 45.4 | 21 | 8 | 38.1 | 18.1 | 61.6 |
| | Grade 3* | 22 | 0 | 0.0 | 0.0 | 15.4 | 21 | 0 | 0.0 | 0.0 | 16.1 |
| | Related* | 22 | 5 | 22.7 | 7.8 | 45.4 | 21 | 8 | 38.1 | 18.1 | 61.6 |
| Malaise | Any | 22 | 2 | 9.1 | 1.1 | 29.2 | 21 | 3 | 14.3 | 3.0 | 36.3 |
| | Grade 3* | 22 | 0 | 0.0 | 0.0 | 15.4 | 21 | 0 | 0.0 | 0.0 | 16.1 |
| | Related* | 22 | 2 | 9.1 | 1.1 | 29.2 | 21 | 3 | 14.3 | 3.0 | 36.3 |
| Myalgia | Any | 22 | 3 | 13.6 | 2.9 | 34.9 | 21 | 3 | 14.3 | 3.0 | 36.3 |
| | Grade 3* | 22 | 0 | 0.0 | 0.0 | 15.4 | 21 | 0 | 0.0 | 0.0 | 16.1 |
| | Related* | 22 | 3 | 13.6 | 2.9 | 34.9 | 21 | 3 | 14.3 | 3.0 | 36.3 |
| Temperature (Oral) | ≥ 37.5 °C | 22 | 1 | 4.5 | 0.1 | 22.8 | 21 | 0 | 0.0 | 0.0 | 16.1 |
| | > 39.5 °C* | 22 | 0 | 0.0 | 0.0 | 15.4 | 21 | 0 | 0.0 | 0.0 | 16.1 |
| | Related* | 22 | 1 | 4.5 | 0.1 | 22.8 | 21 | 0 | 0.0 | 0.0 | 16.1 |

N = number of subjects with the documented dose
n/% = number/percentage of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit
Any = Occurrence of any general symptom regardless of the intensity grade or relationship to vaccination
Grade 3 = symptom that prevented normal activity
Related = general symptom assessed by the investigator to be casually related to the study vaccination
[£]Gastrointestinal symptoms included nausea, vomiting, diarrhoea and/or abdominal pain.
*Primary outcome variable.

Primary Efficacy Results: Number (%) of subjects with haematology and biochemistry abnormalities at Days 1 and 6 after booster vaccination (Total Vaccinated cohort)

| | | | | Grade ≥ 1 | | Grade ≥ 2 | | Grade ≥ 3[£] | | Grade ≥ 4 | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Laboratory test | Group | Timing | N | n | % | n | % | n | % | n | % |
| Alanine aminotransferase (ALT) | PlPh 2 | Day 1 | 21 | 1 | 4.8 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Aspartate aminotransferase (AST) | PlPh 1 | Day 6 | 22 | 1 | 4.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Cholesterol | PlPh 1 | Day 1 | 22 | 3 | 13.6 | 1 | 4.5 | 0 | 0.0 | 0 | 0.0 |
| | | Day 6 | 22 | 2 | 9.1 | 1 | 4.5 | 1 | 4.5 | 0 | 0.0 |
| | PlPh 2 | Day 1 | 21 | 4 | 19.0 | 2 | 9.5 | 1 | 4.8 | 0 | 0.0 |
| | | Day 6 | 21 | 4 | 19.0 | 2 | 9.5 | 1 | 4.8 | 0 | 0.0 |
| Creatine Phosphokinase (CRP) | PlPh 1 | Day 1 | 22 | 3 | 13.6 | 1 | 4.5 | 0 | 0.0 | 0 | 0.0 |
| | | Day 6 | 22 | 2 | 9.1 | 2 | 9.1 | 1 | 4.5 | 0 | 0.0 |
| | PlPh 2 | Day 1 | 21 | 3 | 14.3 | 1 | 4.8 | 0 | 0.0 | 0 | 0.0 |
| | | Day 6 | 21 | 5 | 23.8 | 1 | 4.8 | 0 | 0.0 | 0 | 0.0 |
| Hemoglobin decrease* | PlPh 1 | Day 1 | 22 | 7 | 31.8 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Day 6 | 22 | 10 | 45.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | PlPh 2 | Day 1 | 21 | 7 | 33.3 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | | Day 6 | 21 | 11 | 52.4 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Haemoglobin | PlPh 1 | Day 1 | 22 | 1 | 4.5 | 1 | 4.5 | 0 | 0.0 | 0 | 0.0 |
| | | Day 6 | 22 | 2 | 9.1 | 1 | 4.5 | 0 | 0.0 | 0 | 0.0 |
| | PlPh 2 | Day 1 | 21 | 1 | 4.8 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | | Day 6 | 21 | 2 | 9.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Lactate dehydrogenase (LDH) | PlPh 1 | Day 6 | 22 | 1 | 4.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Neutrophils | PlPh 1 | Day 6 | 22 | 2 | 9.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | PlPh 2 | Day 6 | 21 | 2 | 9.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Red blood cells (RBC) | PlPh 1 | Day 1 | 22 | 7 | 31.8 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | | Day 6 | 22 | 6 | 27.3 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | PlPh 2 | Day 1 | 21 | 5 | 23.8 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | | Day 6 | 21 | 4 | 19.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Reticulocytes | PlPh 1 | Day 6 | 22 | 1 | 4.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| White blood cells (WBC)** | PlPh 1 | Day 1 | 22 | 2 | 9.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | | Day 6 | 22 | 1 | 4.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | PlPh 2 | Day 1 | 21 | 3 | 14.3 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Overall parameters | PlPh 1 | Day 1 | 22 | 14 | 63.6 | 3 | 13.6 | 0 | 0.0 | 0 | 0.0 |
| | | Day 6 | 22 | 17 | 77.3 | 3 | 13.6 | 1 | 4.5 | 0 | 0.0 |
| | PlPh 2 | Day 1 | 21 | 14 | 66.7 | 3 | 14.3 | 1 | 4.8 | 0 | 0.0 |
| | | Day 6 | 21 | 17 | 81.0 | 3 | 14.3 | 1 | 4.8 | 0 | 0.0 |

N = number of subjects with laboratory results at the specific time point.
n/% = number/percentage of subjects with a maximum grade in the given category.
Day 1 = 1 day after booster vaccination.
Day 6 = 7 days after booster vaccination
*Derived parameter counting for change from baseline
**Depending on the subject and the visit, testing of WBC was done as an increase or a decrease.
FDA Toxicity Grading Scale for biochemical parameters:

| | Mild (Grade 1) | Moderate (Grade 2) | Severe (Grade 3) | Potentially Life Threatening (Grade 4)** |
|---|---|---|---|---|
| Liver Function Tests – ALT, AST increase by factor | 1.1 – 2.5 x ULN | 2.6 – 5.0 x ULN | 5.1 – 10 x ULN | > 10 x ULN |
| Creatinine – mg/dL | 1.5 – 1.7 | 1.8 – 2.0 | 2.1 – 2.5 | > 2.5 or requires dialysis |
| Cholesterol | 201 – 210 | 211 – 225 | > 226 | --- |
| Hemoglobin (Female) - gm/dL | 11.0 – 12.0 | 9.5 – 10.9 | 8.0 – 9.4 | < 8.0 |
| Hemoglobin (Female) change from baseline value - gm/dL | Any decrease – 1.5 | 1.6 – 2.0 | 2.1 – 5.0 | > 5.0 |
| Hemoglobin (Male) - gm/dL | 12.5 – 13.5 | 10.5 – 12.4 | 8.5 – 10.4 | < 8.5 |
| Hemoglobin (Male) change from baseline value – gm/dL | Any decrease – 1.5 | 1.6 – 2.0 | 2.1 – 5.0 | > 5.0 |
| Neutrophils Decrease - cell/$mm^3$ | 1,500 – 2,000 | 1,000 – 1,499 | 500 – 999 | < 500 |
| WBC Decrease - cell/$mm^3$ | 2,500 – 3,500 | 1,500 – 2,499 | 1,000 – 1,499 | < 1,000 |
| WBC Increase - cell/$mm^3$ | 10,800 – 15,000 | 15,001 – 20,000 | 20,001 – 25, 000 | > 25,000 |

ULN = upper limit normal
Grades for study required tests not included within the FDA Toxicity Grading Scale:

| | Normal range | Grade 1 | Grade 2 | Grade 3 | Grade 4 (SAE) |
|---|---|---|---|---|---|
| LDH([a]) | 0-220 Units/L | 1-1.5 x ULN([b]) | 1.5-2 x ULN | 2-3 x ULN | > 3 x ULN |
| Reticulocytes index: Male | 0.8-2.5 | 1-1.5 x ULN | 1.5-2 x ULN | 2-3 x ULN | > 3 x ULN |
| Reticulocytes index: Female | 0.8-4.1 | 1-1.5 x ULN | 1.5-2 x ULN | 2-3 x ULN | > 3 x ULN |

ULN = upper limit normal
£Primary outcome variable

**Primary Efficacy Results:** Please refer to the safety section of this CTRS for the results on unsolicited AEs and SAEs.

**Secondary Outcome Variables:** Seropositivity* rates and GMCs for anti-dPly antibodies (ATP cohort for immunogenicity)

| | | | | ≥ 599 LU/mL | | | | GMC (LU/mL) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 95% CI | | | 95% CI | |
| Antibody | Group | Timing | N | n | % | LL | UL | value | LL | UL |
| Anti-dPly | PlPh 1 | PRE-BOOSTER | 22 | 22 | 100 | 84.6 | 100 | 41823.0 | 30264.0 | 57796.7 |
| | | POST-BOOSTER | 22 | 22 | 100 | 84.6 | 100 | 92943.4 | 65790.6 | 131302.6 |
| | PlPh 2 | PRE-BOOSTER | 20 | 20 | 100 | 83.2 | 100 | 89612.2 | 65851.0 | 121947.2 |
| | | POST-BOOSTER | 20 | 20 | 100 | 83.2 | 100 | 144767.0 | 106911.5 | 196026.4 |

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-BOOSTER = blood sample taken before booster vaccination dose
POST-BOOSTER = blood sample 30 days after booster dose
*A seropositive subject was defined as a subject with anti-dPly antibody concentration ≥ 599 LU/mL.

**Secondary Outcome Variables:** Seropositivity* rates and GMTs for Hem-dPly antibodies (ATP cohort for immunogenicity)

| | | | | ≥ 6 | | | | GMT | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 95% CI | | | 95% CI | |
| Antibody | Group | Timing | N | n | % | LL | UL | value | LL | UL |
| Hem-dPly | PlPh 1 | PRE-BOOSTER | 22 | 22 | 100 | 84.6 | 100 | 2161.5 | 1772.1 | 2636.4 |
| | | POST-BOOSTER | 22 | 22 | 100 | 84.6 | 100 | 2383.6 | 1754.4 | 3238.3 |
| | PlPh 2 | PRE-BOOSTER | 20 | 20 | 100 | 83.2 | 100 | 3028.1 | 2210.5 | 4148.1 |
| | | POST-BOOSTER | 20 | 20 | 100 | 83.2 | 100 | 3573.7 | 2561.1 | 4986.5 |

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
GMT = geometric mean titer calculated on all subjects
PRE-BOOSTER = blood sample taken before booster vaccination dose
POST-BOOSTER = blood sample 30 days after booster dose
*A seropositive subject was defined as a subject with Hem-dPly antibody titer ≥ 6

**Secondary Outcome Variables:** Seropositivity* rates and GMCs for anti-PhtD antibodies (ATP cohort for immunogenicity)

| | | | | ≥ 391 LU/mL | | | | GMC (LU/mL) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 95% CI | | | 95% CI | |
| Antibody | Group | Timing | N | n | % | LL | UL | value | LL | UL |
| Anti-PhtD | PlPh 1 | PRE-BOOSTER | 22 | 22 | 100 | 84.6 | 100 | 26672.0 | 19423.7 | 36625.0 |
| | | POST-BOOSTER | 22 | 22 | 100 | 84.6 | 100 | 37850.5 | 29018.1 | 49371.2 |
| | PlPh 2 | PRE-BOOSTER | 20 | 20 | 100 | 83.2 | 100 | 42111.0 | 33408.2 | 53080.9 |
| | | POST-BOOSTER | 20 | 20 | 100 | 83.2 | 100 | 62795.3 | 51695.6 | 76278.3 |

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
GMC = geometric mean antibody concentration calculated on all subjects
PRE-BOOSTER = blood sample at Day 0 before administration of the booster vaccination dose
POST-BOOSTER = blood sample taken 30 days after administration of the booster vaccination dose
*A seropositive subject was defined as a subject with anti-PhtD antibody concentration ≥ 391 LU/mL.

**Safety Results:** Number (%) of subjects with unsolicited AEs during the 31-day (Days 0-30) post-vaccination period (Total Vaccinated cohort)

| Most frequent adverse events - On-Therapy (occurring within Days 0-30 following vaccination) | PlPh 1 Group N = 22 | PlPh 2 Group N = 21 |
|---|---|---|
| Subjects with any AE(s), n (%) | 6 (27.3) | 5 (23.8) |
| Subjects with grade 3 AE(s), n (%) | 1 (4.5) | 1 (4.8) |
| Subjects with related AE(s), n (%) | 1 (4.5) | 1 (4.8) |

| | | |
|---|---|---|
| Diarrhoea | 2 (9.1) | - |
| Headache | 2 (9.1) | - |
| Ear pain | 1 (4.5) | - |
| Aphthous stomatitis | 1 (4.5) | - |
| Oedema peripheral | - | 1 (4.8) |
| Bronchitis | - | 1 (4.8) |
| Pharyngitis | 1 (4.5) | - |
| Pneumonia | - | 1 (4.8) |
| Upper respiratory tract infection | - | 1 (4.8) |
| Back pain | - | 1 (4.8) |
| Oropharyngeal pain | 1 (4.5) | - |
| Uritcaria | - | 1 (4.8) |
| - : Adverse event absent<br>Grade 3 = event which prevented normal activities<br>Related = event assessed by the investigator as causally related to the study vaccination | | |
| Safety Results: Number (%) of subjects with SAEs during the entire study period (Days 0-30) (Total Vaccinated cohort) | | |
| Serious adverse event, n (%) [n considered by the investigator to be related to study medication] | | |
| All SAEs | PIPh 1 Group<br>N = 22 | PIPh 2 Group<br>N = 21 |
| Subjects with any SAE(s), n (%) [n assessed by the investigator as related] | 0 (0.0) [0] | 0 (0.0) [0] |
| Fatal SAEs | PIPh 1 Group<br>N = 22 | PIPh 2 Group<br>N = 21 |
| Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related] | 0 (0.0) [0] | 0 (0.0) [0] |

Conclusion:

During the 7-day (days 0-6) follow-up period after booster vaccination, the most frequently reported solicited local and general symptoms were pain and headache for the PIPh 1 Group and pain and fatigue for the PIPh 2 Group.

During the 31-day (days 0-30) follow-up period after booster vaccination, at least one unsolicited AE was reported for 6 subjects (27.3%) inf the PIPh 1 Group and 5 subjects (23.8%) in the PIPh 2 Group. During the same period, at least one Grade 3 unsolicited AE was reported for 1 (4.5%) subject in the PIPh 1 Group and 1 (4.8%) subject in the PIPh 2 Group, and, similarly, at least one unsolicited AE as assessed by investigator to be causally related to vaccination, was reported for 1 (4.5%) subject in the PIPh 1 Group and 1 (4.8%) subject in the PIPh 2 Group.

At Day 1, 1 (4.5%) subject in the PIPh 1 Group reported grade 3 haematological or biochemical abnormalities. At Day 6, 1 (4.5%) subject in the PIPh 1 Group and 1 (4.8%) subject in the PIPh 2 Group reported grade 3 haematological or biochemical abnormalities.

No SAE (vaccine-related, non-fatal or fatal) was reported during the entire study.

Date updated: 22-September-2014