SYNOPSIS

Name of Company: GlaxoSmithKline Biologicals, Rixensart, Belgium **Name of Finished Product:** **Name of active substance:** **11PCV**	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Title of the study:
A phase I/II, randomized, observer blinded study to evaluate and compare the safety, reactogenicity and immunogenicity of various formulations of the GlaxoSmithKline Biologicals' adjuvanted 11-valent pneumococcal conjugate vaccine versus the licensed single-dose 23-valent pneumococcal polysaccharide vaccine and GlaxoSmithKline Biologicals' aluminium-based 10-valent pneumococcal conjugate vaccine, in healthy elderly subjects.

Principal Investigators:
This study was conducted by 3 investigators in 3 countries (Belgium, Sweden, and Finland):

- Prof. Dr. [redacted] Belgium.
- Dr. [redacted] Finland.
- Dr. [redacted] Sweden.

Study Centres:

- [redacted] Belgium. GSK assigned centre number: [redacted]
- [redacted] Finland. GSK assigned centre number: [redacted]
- [redacted] Sweden. GSK assigned centre number: [redacted]

Publication (reference):
Not published as of Novenber 2007.

Study period:	**Clinical phase:**
Study Initiation Date: 01 June 2006 Date of Last Month 4 Visit: 08 January 2007 Study Completion Date: 08 January 2007 Data Lock point: 11 April 2007	**I/II**

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Objectives:

Primary:

- To assess in healthy elderly subjects the safety and reactogenicity of the 11PCV adjuvanted either with AS01B or AS01E or AS02V, and of the 10-valent pneumococcal conjugate vaccine adjuvanted with $AlPO_4$ (10PCV/$AlPO_4$), given as a 2-dose vaccination 3 months apart, and of the licensed 23-valent pneumococcal polysaccharide vaccine (23PPV) given as a 1-dose vaccination.
- To compare the antibody response of the 11PCV, adjuvanted either with AS01B, AS01E or AS02V, after 1 and 2 injections with the antibody response of the 23PPV.

Secondary:

- To evaluate the safety as measured by haematological and biochemical parameters in each group.
- To evaluate the humoral immune response elicited after 1 or 2 doses of 10PCV/$AlPO_4$, injected at 3 months interval.
- To evaluate the humoral immune response at month 12 in each group.
- To evaluate the B-cell memory response to 4 polysaccharides in all subjects and to 11 polysaccharides in 10 subjects per group at Months 0, 1, 4 and 12.
- To evaluate the humoral immune response to carrier proteins at Months 0, 1, 3, 4 and 12, in the 11PCV/AS01B, 11PCV/AS01E, 11PCV/AS02V and 10PCV/$AlPO_4$ groups.
- To evaluate the B-cell memory response to NTHi protein D at Months 0, 1, 4 and 12, in a subset of subjects (all subjects minus PS B-cell memory subset) of the 11PCV/AS01B, 11PCV/AS01E, 11PCV/AS02V and 10PCV/$AlPO_4$ groups.
- To evaluate the T-cell response to NTHi protein D at Months 0, 1, 4 and 12, in a subset of subjects (all subjects minus PS B-cell memory subset) of the 11PCV/AS01B, 11PCV/AS01E, 11PCV/AS02V and 10PCV/$AlPO_4$ groups.

Note: All objectives at Month 12 will only be evaluated in subjects in the Belgium site. Results up to Month 12 ((106072) (STREP-ELD-011 EXT010 Y1)) will be presented in an Annex report.

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Study design:
This was a phase I/II, observer blind, multicentre, multicountry, randomized controlled study with five parallel groups.

- 11PCV/AS01B group: 66 subjects receiving GSK Biologicals. 11PCV combined with adjuvant AS01B
- 11PCV/AS01E group: 66 subjects receiving GSK Biologicals. 11PCV combined with adjuvant AS01E
- 11PCV/AS02V group: 66 subjects receiving GSK Biologicals. 11PCV combined with adjuvant AS02V
- 23PPV group: 66 subjects receiving 23PPV (control)
- 10PCV/$AlPO_4$ group: 66 subjects receiving GSK Biologicals. 10PCV adjuvanted with $AlPO_4$ (control)

In the 4 groups receiving the GSK Biologicals' vaccines, each subject received 2 doses vaccination at Month 0 and 3. For the group receiving the 23PPV, subjects received one vaccine dose at Month 0 and one placebo dose at Month 3. Blood samples were taken at Months 0, 1, 3, and 4. One additional blood sampling is planned at Month 12 (Note: Results up to Month 12 ((106072) (STREP-ELD-011 EXT010 Y1)) will be presented in an Annex report.).

Number of subjects:
Planned: 330 to reach 66 subjects / group.
Enrolled: 335 in total (66 subjects / 11PCV/AS01B, 67 subjects / 11PCV/AS01E, 67 subjects / 11PCV/AS02V, 66 subjects / 10PCV/$AlPO_4$, 69 subjects / 23PPV).
Completed: 331 in total (65 subjects / 11PCV/AS01B, 67 subjects / 11PCV/AS01E, 67 subjects / 11PCV/AS02V,65 subjects / 10PCV/$AlPO_4$, 67 subjects / 23PPV).
Safety: Total Vaccinated cohort: 335 in total (66 subjects / 11PCV/AS01B, 67 subjects / 11PCV/AS01E, 67 subjects / 11PCV/AS02V, 66 subjects / 10PCV/$AlPO_4$, 69 subjects / 23PPV).
Immunogenicity: According-to-Protocol (ATP) cohort: 325 in total (65 subjects / 11PCV/AS01B, 66 subjects / 11PCV/AS01E, 65 subjects / 11PCV/AS02V, 64 subjects / 10PCV/ $AlPO_4$, 65 subjects / 23PPV).

Diagnosis and criteria for inclusion:
Elderly subjects aged between 65 and 85 years old, in good general health at the time of the first vaccination. Subjects that had never been vaccinated with the 23PPV or any other vaccine against *Streptococcus pneumoniae.*

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Study vaccine, dose, mode of administration, lot no.:

Vaccination schedule/site:

At Day 0 and Month 3, all subjects in the 11PCV adjuvanted groups received one dose of vaccine via an intramuscular injection into the deltoid muscle of the non-dominant arm.

Vaccine composition/ dose/ lot number:

11PCV/AS01B, 11PCV/AS01E and 11PCV/AS02V candidate vaccines formulations:

Protein D carrier: 1 µg of each PS for serotypes 1, 3, 5, 6B, 7F, 9V, 14 and 23F and 3 µg for serotype 4 conjugated to PD.

Tetanus toxoid carrier with AH spacer: 3 µg of capsular PS of serotype 18C conjugated to TT_{AH}.

Diphtheria toxoid carrier: 3 µg of capsular PS of serotype 19F conjugated to DT.

And the adjuvants (500µl), respectively:

- AS01B: liposome-based adjuvant containing MPL and QS21, no preservative
- AS01E (2-fold dilution of AS01B): liposome-based adjuvant containing MPL and QS21, no preservative
- AS02V: containing MPL and QS21, and oil in water emulsion, no preservative

Lot numbers:

11PCV: DSPNA024A, -AS01B: DA1BA003A, -AS01E: DA1EA003A, -AS02V: DA2VA002A.

Reference vaccine, dose and mode of administration, lot number:

Vaccination schedule/site:

At Day 0, all subjects from the 23PPV and the 10PCV/$AlPO_4$ groups received one dose of vaccine. At Month 3, subjects from the 10PCV/$AlPO_4$ group received a second dose of vaccine and subjects from the 23PPV group received one placebo dose. The vaccination was done via an intramuscular injection into the deltoid muscle of the non-dominant arm.

Vaccine composition/ dose/ lot number:

Pneumovax™ or Pneumo 23™ (MSD Sanofi Pasteur): 25 µg each of the *S. pneumoniae* polysaccharide serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, & 33F. (Preservative: phenol 0.25%).

Lot numbers: Pneumovax™, NB38160 (Finland) and Pneumo 23™, Y0902-5 (Sweden and Belgium).

10PCV/$AlPO_4$: Protein D carrier: 1 µg of each PS for serotypes 1, 5, 6B, 7F, 9V, 14 and 23F and 3µg for serotype 4 conjugated to PD. Tetanus toxoid carrier with AH spacer: 3 µg of capsular PS of serotypes 18C conjugated to TT_{AH}. Diphtheria toxoid carrier: 3µg of capsular PS of serotype 19F conjugated to DT. Protein carrier content: ~12 µg PD, ~ 4.5 µg DT, ~ 7 µg TT. 0.5 mg aluminium (Al3+) as aluminium phosphate adjuvant.

Lot number of 10PCV: DSPNA023A

Placebo: NaCl (150 mM).

Lot number: AD02B053A.

Duration of treatment:

Duration of the study: 12 months. Duration up to the 4 month evaluation: 4 months.

Note: For subjects in the Belgian site, 12 months per subject from the first vaccination (Day 0) and for subjects in the other sites, 4 months per subjects from the first vaccination (Day0). (Amended protocol dated 01 June 2007).

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Criteria for evaluation:

The primary objective of the study is to compare the safety and immunogenicity of three 11PCV vaccine formulations with the 23PPV. The sample size was based on immunogenicity. A sample size of 60 subjects per group achieves 80% power to detect a 30% difference in proportion of responders to at least 6 serotypes out of the 11 between at least one 11PCV vaccine formulation and the 23PPV.

***Immunogenicity*:**

- IgG antibody concentration against the different serotypes out of the 11 present in the vaccine was measured by ELISA (cut-off 0.05 µg/mL). The criteria were: post vaccination concentration IgG ≥ 5 µg/mL and fold increase Post/Pre ≥ 2 for at least 6 serotypes (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F) one month after dose 1 and dose 2 for the 11PCV formulations and one month after dose 1 for the 23PPV group. The IgG antibody concentration to serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F was determined for all groups at Months 0, 1, 3, 4 and 12.
- Haematological and biochemical levels within or outside the normal ranges in all groups, at Months 0, 1, 3, 4 and 12.
- The opsonophagocytic activity titres (OPA) against different serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) was determined in all groups at Months 0, 1, 3, 4, and 12. The cut-off value for the OPA assay was 8 dilutions for 50% killing.
- The frequency of PS specific B-cell memory was measured by in vitro cultivated memory B-cells (ELISPOT) at Months 0, 1, 4, and 12 for 4 serotypes (3, 6B, 14, 19F) in all groups and for 11 serotypes (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F) in 10 subjects per group.
- The anti-protein D, anti-tetanus and anti-diphtheria toxoids IgG antibody concentrations were determined by ELISA (cut-off of 100 EL.U/ml for the anti-protein D and 0.1 IU/ml for the two others) at Months 0, 1, 3, 4, and 12 in all groups except the 23PPV group.
- The frequency of protein D specific B-cell memory was measured by in vitro cultivated memory B-cells (ELISPOT) at Months 0, 1, 4, and 12 in a subset of subjects per group in all groups except the 23PPV group.
- The cell-mediated immunity was assessed by the determination of the frequency of CD4+ and CD8+ T-Cells to Protein D by the intracellular cytokine staining assay in a subset of subjects at Months 0, 1, 4, and 12 in all groups except the 23PPV group.

***Safety*:**

Recording of solicited local pain local (pain, redness and swelling) and general (fever, fatigue, headache, gastrointestinal symptoms, malaise, and myalgia) adverse events during a 7-day follow-up period (Day 0 to Day 6) after each vaccine dose. Recording of unsolicited local and general adverse events during a 31-day follow-up period (Day 0 to Day 30) after each dose and all Serious Adverse Events throughout the entire study period.

Note: All objectives at Month 12 will only be evaluated in subjects in the Belgium site. Results up to Month 12 ((106072) (STREP-ELD-011 EXT010 Y1)) will be presented in an Annex report.

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Primary end-points:

- Post vaccination concentration IgG ≥ 5 ug/mL and fold increase Post/Pre ≥ 2 for at least 6 serotypes out of 11 (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F).
- Occurrence, intensity, and relationship to vaccination of solicited and unsolicited symptoms. Recording of SAEs.

Biochemical and haematological analysis were performed at month 0, 1, 3 and 12.

Secondary end-points:

- Haematology and biochemical levels within or outside the normal range.
- IgG antibody concentrations to pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F (ELISA) in all groups.
- Opsonophagocytic activity titres (OPA) for pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F (ELISA) in all groups.
- Frequencies of IgG PS-specific B-memory plasma cells for 4 serotypes (3, 6B, 14, 19F).
- Anti-protein D, anti-tetanus and anti-diphtheria toxoids IgG antibody concentrations.
- Frequencies of IgG protein D-specific B-memory plasma cells.
- Frequencies of CD4+ and CD8+ T cells with antigen-specific IL-2 and/or IFNγ and/or TNFα and/or CD40L secretion/expression to protein D.

Note: All endpoints at Month 12 will only be evaluated in subjects in the Belgium site. Results up to Month 12 ((106072) (STREP-ELD-011 EXT010 Y1)) will be presented in an Annex report.

Statistical methods:

Analyses were performed as per protocol.
The analysis of reactogenicity was performed on the Total Vaccinated cohort, the analysis of immunogenicity was performed on the ATP cohort for immunogenicity.
The percentage of subjects reporting any solicited adverse events within the 7 days following vaccination and their exact 95% confidence interval (CI) were computed by group according to the type of adverse events, their intensity and relationship to vaccination. Unsolicited symptoms were reported within 30 days after each vaccination with exact 95% CI and classified by the Medical Directory for Regulatory Activities (MedDRA).
For each laboratory parameter, the number and percentage of subjects with levels below, within and above normal range were tabulated per group, at each assessed time point. The number and percentage of subjects in each study group who fell into the categories (below, within and above normal range) at any assessment were cross-tabulated with their baseline category. For each study centre, haematological and biochemical levels of each laboratory parameter were summarized per group, at each assessed time point. Graphs of medians (with Q1-Q3) over time were displayed per group.

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Immunogenicity

Between group assessment:

For each adjuvanted 11PCV vaccine formulation, the percentage of responders to at least 6 serotypes out of the 11, post dose 2 (Month 4), was compared to the percentage of responders to at least 6 serotypes out of the 11, post dose 1 (Month 1), of 23PPV. A subject was considered to be a responder for a particular serotype if the post vaccination anti-polysaccharides antibody concentration ≥ 5 ug/ml and the fold increase post/pre (Month 0) ≥ 2. Two-sided asymptotic p-values less than 0.0166 were considered as significant. Associated standardized asymptotic confidence intervals (1-0.0166=98.3%) for differences in proportions were computed.

Within group assessment:

ELISA data

Percentage of responders, seropositivity rates, and geometric mean concentrations (GMC) with 95% CI were tabulated per group and per serotype/antigen, at each assessed time point.

A vertical bar chart showing the percentage of responders to at least 6 serotypes out of the 11, one month post dose 1 and 2 for each group except 23PPV and, one month post dose 1 for 23PPV was presented. For each serotype/antigen, the distribution of antibody concentrations after each vaccine administration was displayed using reverse cumulative curves. GMCs over time were also plotted.

OPA data

Seropositivity rates and the geometric mean titres (GMT) with 95% CI were tabulated per group and per serotype, at each assessed time point. For each serotype, the distributions of opsonophagocytic titres after each vaccine administration were displayed using reverse cumulative curves. GMTs over time were also plotted.

ELISPOT data

Frequency of PS-specific plasma cells and NTHi protein D-specific plasma cells were summarized per group, at each assessed time point. Data were also displayed using boxplots.

ICS data

At each assessed time point, the following parameters were tabulated per treatment group:
the frequency of protein D specific CD4/CD8 T-lymphocytes per 10^6 producing at least

- two different cytokines (IL-2, IFN-γ, TNF-α, CD40L)
- IL-2 and another cytokine (IFN-γ, TNF-α, CD40L)
- IFN-γ and another cytokine (IL-2, TNF-α, CD40L)
- TNF-α and another cytokine (IL-2, IFN-γ, CD40L)
- CD40L and another cytokine (IL-2, IFN-γ, TNF-α).

Data were also displayed using boxplots.

In addition, stratified analyses by age group (< 70 year olds versus ≥ 70 year olds) were performed for all immunological endpoints described above.

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Summary:

Demography Results:
The mean age at the time of first vaccination was 69.3 years (range: 65 to 83), there were approximately the same number of male and female subjects and the population was of white/Caucasian origin with the exception of one subject of Asian origin. The demographic profile of the 5 groups of subjects was comparable with respect to mean age and gender.

Immunogenicity Results:
Analysis of immunogenicity was performed on the ATP cohort for immunogenicity.

Immunogenicity to pneumococcal serotypes in all groups

Within group assessment:
The highest percentages of responders one month post last vaccine dose, post dose 2 (Month 4), were observed for the serotypes, PS18C and PS19F (65.6-100% and 66.1 -83.3%, respectively). The serotypes PS1, PS4, PS5, PS6B, PS7F, PS9V, PS14 and PS23F had moderate percentages of responders and few or no subjects were seropositive for anti-PS3.

Between group assessment:
The post dose 1 (Month 1) percentage of responders was comparable for all serotypes between the 11PCV vaccine formulations, 11AS01B, 11AS01E and 11AS02V groups (range 30.8% to 50.0%) and to the control group 23PPV (43.1%).
The post dose 2 (Month 4) percentage of responders to at least 6 serotypes of the 11 was comparable between groups 11AS01B (35.4%), 11AS01E (43.9%) and 11AS02V (36.9%) and to the control 23PPV (43.1% post dose 1). No increase of responders was observed post dose 2 (Month 4) versus post dose 1 (Month 1). No 2-dose 11PCV vaccine formulation was found to be significantly better than 23PPV

Anti-PS antibody reponse by Elisa (Within group assessment):
Post dose 1 (Month 1), depending on the serotype most of subjects (85.7% to 100%) were seropositive for each of the 13 serotypes. No differences were observed post dose 2 (Month 4), as depending on the serotype, 83.9% to 100% of the subjects were seropositive. Age did not seem to have an impact on seropositivity rates.
When comparing the post dose 2 adjuvanted 11PCV vaccine formulation groups to the control 23PPV group (post dose 1), only for 2 serotypes (serogroups 18C and 19F) was there an increase in antibody response observed. In the 11AS02V group, the increase in antibody response, for these two serotypes, was higher than for the 11AS01B and 11AS01E groups. The anti-18C GMC increased 4-6 fold, whilst the anti-19F GMC increased < 2 fold.

Opsonophagocytic avtivity (OPA) (Within group assessment):
Post dose 1 (Month 1), depending on the serotype, 72.3 to 100% of the subjects had antibody titreș ≥ 1:8. Post dose 2 (Month 2), for each individual serotype, 73.8 to 100% of the subjects had antibody titerș ≥ 1:8. For only 2 polysaccharides (serogroups 18C and 19F) was there a superior response in GMTs observed, when comparing the 11PCV vaccine formulation groups (post dose 2) to the 23PPV group (post dose 1). In the 11AS02V group, the increase in antibody response, for these two serotypes, was higher than for the 11AS01B and 11AS01E groups. The anti-18C GMT was 7-11 fold higher, whilst the anti-19F GMT was 2-4 fold higher.

B memory response by Elispot (Within group assessment):
The B Memory response was measured only for serotypes 3, 6B, 14 and 19F. Elispot data were highly variable whatever the serotype, the treatment group or the time point. A good response was only observed to the PS19F serotype when vaccinating with the 11AS01B or 11AS02V vaccines compared to the $10AlPO_4$ and 23PPV vaccines (a 5-6 fold increase in medians was observed between pre-vaccination and post dose 2). Age did not seem to impact on the frequency on PS-specific memory B cells.

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Immunogenicity to carrier proteins in all groups except 23PPV
Antibody reponse by Elisa:
Post vaccination, most subjects, in all groups, were seropositive for anti-protein D antibodies (96.1-100%), anti-tetanus toxoid antibodies (86-100%) and anti-diphtheria toxoid antibodies (59.6-90.4%).

B memory response by Elispot:
The frequency of NTHi protein D-specific memory B cells was similar between the three adjuvanted 11PCV formulation groups and the 10$AlPO_4$ group. No response was observed to protein D. Age did not seem to impact on the frequency of PS-specific memory B cells.

CD4/CD8 responses by Intracellular Staining (ICS)
No adjuvant effect on CD4 response to protein D was observed. The adjuvanted 11PCV vaccines formulation groups were comparable to the 10PCV vaccine adjuvanted with $AlPO_4$. No CD8 response was detected.

Safety Results:
Safety analyses were performed on the Total Vaccinated cohort only.

Serious Adverse Events:
7 subjects reported 8 SAEs (2 in each group 11AS01B, 11AS01E and 23PPV, 1 in group 11AS02V and none in the 10$AlPO_4$ group). None of these SAEs were considered to be causally related to vaccination by the investigator.

[redacted] This SAE was not considered by the investigator to be possibly related to the study vaccination.

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Withdrawals due to adverse events/serious adverse events:
Out of the 335 enrolled subjects, two subjects withdrew from the study due to an SAE: [redacted] Both SAEs were not considered by the investigator to be related to the vaccination. [redacted]

Conclusions:
No adjuvanted 11PCV vaccine formulation was shown to be significantly superior to the 23PPV vaccine in terms of percentage of responders for any serotype as defined by a post vaccination concentration of anti-PS IgG antibody response IgG ≥ 5 ug/mL and fold increase Post/Pre ≥ 2 (ELISA).

For the primary end-point, the percentages of responders to at least 6/11 serotypes (Post vaccination concentration IgG ≥ 5 ug/mL and fold increase Post/Pre ≥ 2 for at least 6 serotypes out of 11 (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F (ELISA)), one month after dose 2 for the 11PCV formulations were not superior to those observed one month after dose 1 for the 23PPV group.

Only for two serotypes 18C and 19F, conjugated to the tetanus and diphtheria toxoids carrier proteins respectively, was the anti-PS response (GMC) higher in the 11PCV vaccine formulations compared to the 23PPV group. For all serotypes coupled with protein D, there was no difference in anti-PS response between the 11PCV vaccine formulations and the 23PPV control group.

No significant increase in anti-PS antibody response was observed in the 11PCV vaccine formulations post dose 2 versus post dose 1.

The same pattern was observed for the opsonophagocytic activity.

A good B Memory response by ELISPOT was observed for the serotype 19F when vaccinating with the 11AS01B or 11AS02V groups (a 5-6 fold increase in medians was observed between pre-vaccination and post dose 2). No B memory response was measured for the other assessed serotypes 3, 6B and 14.

Anti-PS antibody and B cell responses tended to be higher for the 11PCV vaccine formulation adjuvanted with AS02V than in the two other 11PCV vaccine formulations.

The response to the carrier proteins was also measured. The antibody response to protein D (PD) increased after one injection but not after the second with no differences between the 11PCV vaccine formulation groups and the $10AlPO_4$ group. The same pattern was observed for the cellular response by ICS. Vaccination did not induce any B memory response to PD. There was a weak antibody response to the tetanus and diphtheria toxoid carrier proteins.

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All vaccine formulations were well tolerated.

There was a trend towards higher reactogenicity for the adjuvanted 11PCV vaccine formulations compared to the control vaccines, $10AlPO_4$ and 23PPV.

No major differences were observed between the three adjuvanted 11PCV vaccine formulations.

No increase in the incidence of solicited and unsolicited symptoms after two doses compared to one dose could be detected with the exception for redness, as more grade 3 redness symptoms were reported after the second dose as compared to the first dose in the 11PCV groups adjuvanted with AS01B or AS02V.

In conclusion, no difference in anti-PS antibody response was observed between the 3 adjuvanted 11PCV vaccines and the two control groups (23PPV and $10AlPO_4$) for all serotypes coupled with the protein D. A strongly increased response was detected for the serotype 18C coupled on tetanus toxoid (TT), and to a lesser extent for the serotype 19F coupled on diphteria toxoid (DT). Despite a trend for more frequent adverse reactions in the 11PCV vaccine formulation groups, all vaccine formulations were well tolerated.

Date of report: November 2007