Clinical trial results:
Antibody persistence in healthy South African children after primary series and booster vaccination with an investigational (DTaP-IPV-Hep B-PRP-T) or control vaccines

Summary

EudraCT number	2011-004450-26
Trial protocol	Outside EU/EEA
Global end of trial date	07 September 2011

Results information

Result version number	v1 (current)
This version publication date	10 February 2016
First version publication date	20 November 2014

Trial information

Trial identification

Sponsor protocol code	A3L26

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01105559
WHO universal trial number (UTN)	U1111-1111-5789

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, Avenue Pont Pasteur, Lyon Cedex 07, France, F-69367
Public contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 5843, emmanuel.feroldi@sanofipasteur.com
Scientific contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (0)4 37 37 5843, emmanuel.feroldi@sanofipasteur.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001201-PIP01-11
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 May 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the antibody long term persistence at 3.5 and 4.5 years of age following a 3-dose primary series vaccination of either DTaP-IPV-Hep B-PRP-T or CombAct-Hib™ + oral poliovirus vaccine (OPV) + Engerix™ B vaccination at 6, 10, and 14 weeks of age and a booster vaccination of DTaP-IPV-Hep B-PRP-T or CombAct-Hib™ + OPV at 15-18 months

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment were also available on site in case of any immediate allergic reactions.

Background therapy:

Study participants must have been enrolled in a previous study, A3L15 and completed a 3-dose primary series vaccination of either DTaP-IPV-Hep B-PRP-T or CombAct-Hib+oral poliovirus vaccine (OPV)+Engerix B vaccination at 6, 10 and 14 weeks of age and a booster vaccination of DTaP-IPV-Hep B-PRP-T or CombAct-Hib+OPV at 15 to 18 months.

Evidence for comparator:

Not applicable

Actual start date of recruitment	29 April 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	South Africa: 453
Worldwide total number of subjects	453
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	453
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled from 29 April 2010 to 07 September 2011 in 2 clinical centers in Republic of South Africa.

Pre-assignment

Screening details:

A total of 567 subjects included in the primary and booster series of study A3L15 were invited to participate in the current study, A3L26. Four hundered and fifty five (455) subjects were enrolled at visit 1, 2 were withdrawn for protocol violation.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

Subjects who previously received DTaP-IPV-Hep B-PRP-T vaccine for primary and booster series vaccinations in A3L15 study.

Arm type	Experimental
Investigational medicinal product name	Hexaxim
Investigational medicinal product code	DTaP-IPV-HepB-PRP-T vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

No vaccination was administered as part of this study.

Arm title	Group 2

Arm description:

Subjects who previously received DTwP-Hib (CombAct-Hib) + Hep B (Engerix B) + oral poliovirus vaccines (OPV) for primary series vaccinations and CombAct-Hib + OPV as a booster vaccine in study A3L15.

Arm type	Active comparator
Investigational medicinal product name	CombAct-Hib™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular injection into the anterolateral area of the right thigh, previously injected in A3L15 at primary series and booster vaccinations.

Investigational medicinal product name	Engerix B™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:	
No vaccination was administered as part of this study.	
Investigational medicinal product name	OPVERO (Oral Poliomyelitis Vaccine)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
No vaccination was administered as part of this study.	
Arm title	Group 3
Arm description:	
Subjects who previously received DTaP-IPV-Hep B-PRP-T + Hep B at birth vaccines for primary series vaccinations and DTaP-IPV-Hep B-PRP-T as a booster in study A3L15.	
Arm type	Active comparator
Investigational medicinal product name	Hexaxim
Investigational medicinal product code	DTaP-IPV-HepB-PRP-T vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL, intramuscular injection into the anterolateral area of the right thigh, previously injected in A3L15 at primary series and booster vaccinations.	
Investigational medicinal product name	Engerix B™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL, intramuscular injection into the anterolateral area of the left thigh, previously injected in A3L15 at birth	

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	173	177	103
Completed	167	167	102
Not completed	6	10	1
Consent withdrawn by subject	3	3	1
Lost to follow-up	3	7	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1
Reporting group description:	
Subjects who previously received DTaP-IPV-Hep B-PRP-T vaccine for primary and booster series vaccinations in A3L15 study.	
Reporting group title	Group 2
Reporting group description:	
Subjects who previously received DTwP-Hib (CombAct-Hib) + Hep B (Engerix B) + oral poliovirus vaccines (OPV) for primary series vaccinations and CombAct-Hib + OPV as a booster vaccine in study A3L15.	
Reporting group title	Group 3
Reporting group description:	
Subjects who previously received DTaP-IPV-Hep B-PRP-T + Hep B at birth vaccines for primary series vaccinations and DTaP-IPV-Hep B-PRP-T as a booster in study A3L15.	

Reporting group values	Group 1	Group 2	Group 3
Number of subjects	173	177	103
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	173	177	103
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	43.4	43.4	43.2
standard deviation	± 0.967	± 0.994	± 0.994
Gender categorical Units: Subjects			
Female	92	82	49
Male	81	95	54

Reporting group values	Total		
Number of subjects	453		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		

Children (2-11 years)	453		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: months			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	223		
Male	230		

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description:	
Subjects who previously received DTaP-IPV-Hep B-PRP-T vaccine for primary and booster series vaccinations in A3L15 study.	
Reporting group title	Group 2
Reporting group description:	
Subjects who previously received DTwP-Hib (CombAct-Hib) + Hep B (Engerix B) + oral poliovirus vaccines (OPV) for primary series vaccinations and CombAct-Hib + OPV as a booster vaccine in study A3L15.	
Reporting group title	Group 3
Reporting group description:	
Subjects who previously received DTaP-IPV-Hep B-PRP-T + Hep B at birth vaccines for primary series vaccinations and DTaP-IPV-Hep B-PRP-T as a booster in study A3L15.	

Primary: Percentage of Subjects Achieving the Predefined Antibody Thresholds for Vaccine Antigens at Age 3.5 Years old and at Age 4.5 Years old Following Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™ B

End point title	Percentage of Subjects Achieving the Predefined Antibody Thresholds for Vaccine Antigens at Age 3.5 Years old and at Age 4.5 Years old Following Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™ B[1]

End point description:

Anti-diphtheria antibodies were measured by a toxin neutralization test. Anti-tetanus, anti-pertussis toxin (PT), and anti-filamentous hemagglutinin (FHA) antibodies were measured by enzyme-linked immunosorbent assay (ELISA). Anti-hepatitis B (Hep B) antibodies were measured by VITROS ECi/ECiQ Immunodiagnostic System using chemiluminescence detection technology. Anti-Haemophilus influenzae type b capsular polyribosyl ribitol phosphate (PRP) antibody concentrations were measured using a Farr-type radioimmunoassay (RIA). Lower limit of quantitation (LLOQ) values for anti-PT and anti-FHA was 2 EU/mL. Subjects vaccinated in Study A3L15 were assessed at Year 1 (Visit 01) defined as the first time point of follow-up at about 2 years (Month 24 to Month 27) post-booster vaccination, when subjects were aged 3.5 years and also at Year 2 (Visit 02) defined as the second time point of follow-up at about 3 years (Month 36 to Month 39) post-booster vaccination, when subjects were aged 4.5 years.

End point type	Primary

End point timeframe:

Month 24 to Month 27 and Month 36 to Month 39 post-booster dose

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	173	177	103	
Units: Percentage of subjects				
number (not applicable)				
Anti-Diphtheria; Year 1-V01 (≥0.01 IU/mL)	98.8	91.5	98.1	
Anti-Diphtheria; Year 1-V01 (≥0.1 IU/mL)	81.3	47.2	68.9	

Anti-Diphtheria; Year 1-V01 (≥1.0 IU/mL)	32.7	2.8	24.3	
Anti-Diphtheria; Year 2-V02 (≥0.01 IU/mL)	98.2	87.5	97	
Anti-Diphtheria; Year 2-V02 (≥0.1 IU/mL)	75.3	33.1	64.4	
Anti-Diphtheria; Year 2-V02 (≥1.0 IU/mL)	18.7	0	24.8	
Anti-Tetanus; Year 1-V01 (≥0.01 IU/mL)	100	100	100	
Anti-Tetanus; Year 1-V01 (≥0.1 IU/mL)	94.7	93.7	94.1	
Anti-Tetanus; Year 1-V01 (≥1.0 IU/mL)	38.2	8.6	36.6	
Anti-Tetanus; Year 2-V02 (≥0.01 IU/mL)	100	100	100	
Anti-Tetanus; Year 2-V02 (≥0.1 IU/mL)	89.5	84.5	82.8	
Anti-Tetanus; Year 2-V02 (≥1.0 IU/mL)	26.5	3.2	20.2	
Anti-PT; Year 1-V01 (≥LLOQ)	95.9	86.7	90	
Anti-PT; Year 1-V01 (≥2xLLOQ)	87.1	80.9	77	
Anti-PT; Year 1-V01 (≥4xLLOQ)	60.6	55.5	52	
Anti-PT; Year 2-V02 (≥LLOQ)	83.6	80.1	78.5	
Anti-PT; Year 2-V02 (≥2xLLOQ)	74	69.5	54.8	
Anti-PT; Year 2-V02 (≥4xLLOQ)	42.5	44.4	23.7	
Anti-FHA; Year 1-V01 (≥LLOQ)	100	99.4	100	
Anti-FHA; Year 1-V01 (≥2xLLOQ)	99.4	92.4	100	
Anti-FHA; Year 1-V01 (≥4xLLOQ)	97.7	70.8	95	
Anti-FHA; Year 2-V02 (≥LLOQ)	100	94.8	100	
Anti-FHA; Year 2-V02 (≥2xLLOQ)	100	86.3	97	
Anti-FHA; Year 2-V02 (≥4xLLOQ)	93.8	62.1	89	
Anti-Hep B; Year 1-V01 (≥10 mIU/mL)	76.3	72.7	96.1	
Anti-Hep B; Year 1-V01 (≥100 mIU/mL)	49.1	22.2	86.4	
Anti-Hep B; Year 2-V02 (≥10 mIU/mL)	73.3	68.5	96.1	
Anti-Hep B; Year 2-V02 (≥100 mIU/mL)	40	17	84.3	
Anti-PRP; Year 1-V01 (≥0.15 µg/mL)	98.3	99.4	99	
Anti-PRP; Year 1-V01 (≥1.0 µg/mL)	87.9	87	89.3	
Anti-PRP; Year 2-V02 (≥0.15 µg/mL)	98.8	98.8	100	
Anti-PRP; Year 2-V02 (≥1.0 µg/mL)	84.7	84.1	78.4	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Antibodies Against Vaccine Antigens at Age 3.5 Years and 4.5 Years old Following Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™ B in a Previous Study

End point title	Geometric Mean Titers (GMTs) of Antibodies Against Vaccine Antigens at Age 3.5 Years and 4.5 Years old Following Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™ B in a Previous Study[2]

End point description:

Anti-diphtheria antibodies were measured by a toxin neutralization test. Anti-tetanus, anti-pertussis toxin (PT), and anti-filamentous hemagglutinin (FHA) antibodies were measured by enzyme-linked

immunosorbent assay (ELISA). Anti-hepatitis B (Hep B) antibodies were measured by VITROS ECi/ECiQ Immunodiagnostic System using chemiluminescence detection technology. Anti-Haemophilus influenzae type b capsular polyribosyl ribitol phosphate (PRP) antibody concentrations were measured using a Farr-type radioimmunoassay (RIA). Subjects vaccinated in Study A3L15 were assessed at Year 1 (Visit 01) defined as the first time point of follow-up at about 2 years (Month 24 to Month 27) post-booster vaccination, when subjects were aged 3.5 years and also at Year 2 (Visit 02) defined as the second time point of follow-up at about 3 years (Month 36 to Month 39) post-booster vaccination, when subjects were aged 4.5 years.

End point type	Primary

End point timeframe:

Month 24 to Month 27 and Month 36 to Month 39 post-booster dose

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	173	177	103	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Diphtheria; Year 1-V01	0.437 (0.344 to 0.556)	0.086 (0.069 to 0.107)	0.244 (0.175 to 0.342)	
Anti-Diphtheria; Year 2-V02	0.272 (0.214 to 0.345)	0.048 (0.038 to 0.061)	0.222 (0.155 to 0.319)	
Anti-Tetanus; Year 1-V01	0.703 (0.594 to 0.831)	0.371 (0.329 to 0.418)	0.588 (0.473 to 0.731)	
Anti-Tetanus; Year 2-V02	0.489 (0.411 to 0.583)	0.246 (0.213 to 0.283)	0.343 (0.273 to 0.43)	
Anti-PT; Year 1-V01	10.8 (9.17 to 12.7)	8.82 (7.34 to 10.6)	7.09 (5.73 to 8.76)	
Anti-PT; Year 2-V02	6.68 (5.43 to 8.21)	6.09 (5.02 to 7.39)	4.27 (3.38 to 5.41)	
Anti-FHA; Year 1-V01	68.4 (58 to 80.7)	17 (14 to 20.7)	60.4 (46.8 to 78)	
Anti-FHA; Year 2-V02	46.3 (39.3 to 54.5)	14.1 (11.2 to 17.7)	33.3 (26.8 to 41.4)	
Anti-Hep B; Year 1-V01	76.3 (54.1 to 108)	30 (23.8 to 37.7)	1175 (756 to 1827)	
Anti-Hep B; Year 2-V02	54 (38.8 to 75.3)	22.6 (17.7 to 28.9)	882 (567 to 1373)	
Anti-PRP; Year 1-V01	4.96 (3.98 to 6.18)	4.33 (3.59 to 5.22)	4.44 (3.31 to 5.95)	
Anti-PRP; Year 2-V02	4.14 (3.34 to 5.13)	3.48 (2.83 to 4.3)	3.34 (2.56 to 4.37)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Anti-diphtheria Immunogenicity Response at Primary Series Vaccinations, at Age 3.5 Years and Age 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™ B

End point title	Percentage of Subjects with Anti-diphtheria Immunogenicity Response at Primary Series Vaccinations, at Age 3.5 Years and Age 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™ B[3]

End point description:

Anti-diphtheria (D) antibodies were measured by a toxin neutralization test. Subjects vaccinated in Study A3L15 were assessed at Year 1 (Visit 01) defined as the first time point of follow-up at about 2 years (Month [M] 24 to M27) post-booster vaccination, when subjects were aged 3.5 years and also at Year 2 (Visit 02) defined as the second time point of follow-up at about 3 years (M36 to M39) post-booster vaccination, when subjects were aged 4.5 years.

End point type	Primary

End point timeframe:

Month 24 to Month 27 and Month 36 to Month 39 post-booster dose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	173	177	103	
Units: Percentage of subjects				
number (not applicable)				
Anti-D; A3L15 Primary (D126; ≥0.01 IU/mL)	96.9	95.3	95.1	
Anti-D; A3L15 Primary (D126; ≥0.1 IU/mL)	39.8	14.6	36.3	
Anti-D; A3L15 Primary (D126; ≥1.0 IU/mL)	1.2	0	2	
Anti-D; A3L15 Pre-Booster (D540; ≥0.01 IU/mL)	92.2	85.1	84.5	
Anti-D; A3L15 Pre-Booster (D540; ≥0.1 IU/mL)	29.9	10.9	35.9	
Anti-D; A3L15 Pre-Booster (D540; ≥1.0 IU/mL)	1.2	0	0	
Anti-D; A3L15 Post-Booster (D570; ≥0.01 IU/mL)	100	100	100	
Anti-D; A3L15 Post-Booster (D570; ≥0.1 IU/mL)	100	98.3	100	
Anti-D; A3L15 Post-Booster (D570; ≥1.0 IU/mL)	97.6	92	92.8	
Anti-D; A3L26 Year 1-V01 (M24 to M27; ≥0.01 IU/mL)	98.8	91.5	98.1	
Anti-D; A3L26 Year 1-V01 (M24 to M27; ≥0.1 IU/mL)	81.3	47.2	68.9	
Anti-D; A3L26 Year 1-V01 (M24 to M27; ≥1.0 IU/mL)	32.7	2.8	24.3	
Anti-D; A3L26 Year 2-V02 (M36 to M39; ≥0.01 IU/mL)	98.2	87.5	97	
Anti-D; A3L26 Year 2-V02 (M36 to M39; ≥0.1 IU/mL)	75.3	33.1	64.4	
Anti-D; A3L26 Year 2-V02 (M36 to M39; ≥1.0 IU/mL)	18.7	0	24.8	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Anti-tetanus Immunogenicity Response at Primary Series Vaccinations, at Age 3.5 Years and at Age 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T combined vaccine or CombAct-Hib™ and OPV and Engerix™ B.

End point title	Percentage of Subjects with Anti-tetanus Immunogenicity Response at Primary Series Vaccinations, at Age 3.5 Years and at Age 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T combined vaccine or CombAct-Hib™ and OPV and Engerix™ B.[4]

End point description:

Anti-tetanus (T) antibodies were measured by enzyme-linked immunosorbent assay (ELISA). Subjects vaccinated in Study A3L15 were assessed at Year 1 (Visit 01) defined as the first time point of follow-up at about 2 years (Month [M] 24 to M27) post-booster vaccination, when subjects were aged 3.5 years and also at Year 2 (Visit 02) defined as the second time point of follow-up at about 3 years (M36 to M39) post-booster vaccination, when subjects were aged 4.5 years.

End point type	Primary

End point timeframe:

Month 24 to Month 27 and Month 36 to Month 39 post-booster dose

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	173	177	103	
Units: Percentage of subjects				
number (not applicable)				
Anti-T; A3L15 Primary (D126; ≥0.01 IU/mL)	100	100	100	
Anti-T; A3L15 Primary (D126; ≥0.1 IU/mL)	100	100	100	
Anti-T; A3L15 Primary (D126; ≥1.0 IU/mL)	74.3	81.6	64.7	
Anti-T; A3L15 Pre-Booster (D540; ≥0.01 IU/mL)	100	100	100	
Anti-T; A3L15 Pre-Booster (D540; ≥0.1 IU/mL)	74.8	90.6	65	
Anti-T; A3L15 Pre-Booster (D540; ≥1.0 IU/mL)	6.7	8.8	3.9	
Anti-T; A3L15 Post-Booster (D570; ≥0.01 IU/mL)	100	100	100	
Anti-T; A3L15 Post-Booster (D570; ≥0.1 IU/mL)	100	100	100	
Anti-T; A3L15 Post-Booster (D570; ≥1.0 IU/mL)	97.6	99.4	97	
Anti-T; A3L26 Year 1-V01 (M24 to M27; ≥0.01 IU/mL)	100	100	100	
Anti-T; A3L26 Year 1-V01 (M24 to M27; ≥0.1 IU/mL)	94.7	93.7	94.1	
Anti-T; A3L26 Year 1-V01 (M24 to M27; ≥1.0 IU/mL)	38.2	8.6	36.6	
Anti-T; A3L26 Year 2-V02 (M36 to M39; ≥0.01 IU/mL)	100	100	100	

Anti-T; A3L26 Year 2-V02 (M36 to M39; ≥0.1 IU/mL)	89.5	84.5	82.8	
Anti-T; A3L26 Year 2-V02 (M36 to M39; ≥1.0 IU/mL)	26.5	3.2	20.2	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Anti-pertussis Immunogenicity Response at Primary Series Vaccinations at Age 3.5 Years and at Age 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™ B

End point title	Percentage of Subjects with Anti-pertussis Immunogenicity Response at Primary Series Vaccinations at Age 3.5 Years and at Age 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™ B[5]

End point description:

Anti-pertussis toxin (PT) antibodies were measured by enzyme-linked immunosorbent assay (ELISA). Lower limit of quantitation (LLOQ) values for anti-PT was 2 EU/mL. Subjects vaccinated in Study A3L15 were assessed at Year 1 (Visit 01) defined as the first time point of follow-up at about 2 years (Month [M] 24 to M27) post-booster vaccination, when subjects were aged 3.5 years and also at Year 2 (Visit 02) defined as the second time point of follow-up at about 3 years (M36 to M39) post-booster vaccination, when subjects were aged 4.5 years.

End point type	Primary

End point timeframe:

Month 24 to Month 27 and Month 36 to Month 39 post-booster dose

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	173	177	103	
Units: Percentage of subjects				
number (not applicable)				
Anti-PT; A3L15 Primary (D126; ≥LLOQ)	100	99.2	100	
Anti-PT; A3L15 Primary (D126; ≥2xLLOQ)	100	98.4	100	
Anti-PT; A3L15 Primary (D126; ≥4xLLOQ)	100	94.5	100	
Anti-PT; A3L15 Pre-Booster (D540; ≥LLOQ)	98.6	83.9	97.8	
Anti-PT; A3L15 Pre-Booster (D540; ≥2xLLOQ)	91.6	72.6	88.9	
Anti-PT; A3L15 Pre-Booster (D540; ≥4xLLOQ)	63.6	64.5	60	
Anti-PT; A3L15 Post-Booster (D570; ≥LLOQ)	100	93.9	100	
Anti-PT; A3L15 Post-Booster (D570; ≥2xLLOQ)	100	93.3	100	
Anti-PT; A3L15 Post-Booster (D570; ≥4xLLOQ)	100	92.7	100	

Anti-PT; A3L26 Year 1-V01 (M24 to M27; ≥LLOQ)	95.9	86.7	90	
Anti-PT; A3L26 Year 1-V01 (M24 to M27; ≥2xLLOQ)	87.1	80.9	77	
Anti-PT; A3L26 Year 1-V01 (M24 to M27; ≥4xLLOQ)	60.6	55.5	52	
Anti-PT; A3L26 Year 2-V02 (M36 to M39; ≥LLOQ)	83.6	80.1	78.5	
Anti-PT; A3L26 Year 2-V02 (M36 to M39; ≥2xLLOQ)	74	69.5	54.8	
Anti-PT; A3L26 Year 2-V02 (M36 to M39; ≥4xLLOQ)	42.5	44.4	23.7	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Anti-Filamentous Hemagglutinin Response at Primary Series Vaccinations, at Age 3.5 Years and 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™ B.

End point title	Percentage of Subjects with Anti-Filamentous Hemagglutinin Response at Primary Series Vaccinations, at Age 3.5 Years and 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™ B.[6]

End point description:

Anti- filamentous hemagglutinin (FHA) antibodies were measured by enzyme-linked immunosorbent assay (ELISA). Lower limit of quantitation (LLOQ) values for anti-FHA was 2 EU/mL. Subjects vaccinated in Study A3L15 were assessed at Year 1 (Visit 01) defined as the first time point of follow-up at about 2 years (Month [M] 24 to M27) post-booster vaccination, when subjects were aged 3.5 years and also at Year 2 (Visit 02) defined as the second time point of follow-up at about 3 years (M36 to M39) post-booster vaccination, when subjects were aged 4.5 years.

End point type	Primary

End point timeframe:

Month 24 to Month 27 and Month 36 to Month 39 post-booster dose

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	173	177	103	
Units: Percentage of subjects				
number (not applicable)				
Anti-FHA; A3L15 Primary (D126; ≥LLOQ)	100	100	100	
Anti-FHA; A3L15 Primary (D126; ≥2xLLOQ)	100	100	100	
Anti-FHA; A3L15 Primary (D126; ≥4xLLOQ)	100	97.6	100	
Anti-FHA; A3L15 Pre-Booster (D540; ≥LLOQ)	100	87.9	100	

Anti-FHA; A3L15 Pre-Booster (D540; ≥2xLLOQ)	97.4	65.9	100	
Anti-FHA; A3L15 Pre-Booster (D540; ≥4xLLOQ)	89.4	34.1	86.5	
Anti-FHA; A3L15 Post-Booster (D570; ≥LLOQ)	100	100	100	
Anti-FHA; A3L15 Post-Booster (D570; ≥2xLLOQ)	100	100	100	
Anti-FHA; A3L15 Post-Booster (D570; ≥4xLLOQ)	100	100	100	
Anti-FHA; A3L26 Year 1-V01 (M24 to M27; ≥LLOQ)	100	99.4	100	
Anti-FHA; A3L26 Year 1-V01 (M24 to M27; ≥2xLLOQ)	99.4	92.4	100	
Anti-FHA; A3L26 Year 1-V01 (M24 to M27; ≥4xLLOQ)	97.7	70.8	95	
Anti-FHA; A3L26 Year 2-V02 (M36 to M39; ≥LLOQ)	100	94.8	100	
Anti-FHA; A3L26 Year 2-V02 (M36 to M39; ≥2xLLOQ)	100	86.3	97	
Anti-FHA; A3L26 Year 2-V02 (M36 to M39; ≥4xLLOQ)	93.8	62.1	89	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Anti-hepatitis B Immunogenicity Response at Primary Series Vaccination at Age 3.5 Years and at Age 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™B

End point title	Percentage of Subjects with Anti-hepatitis B Immunogenicity Response at Primary Series Vaccination at Age 3.5 Years and at Age 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T Combined Vaccine or CombAct-Hib™ and OPV and Engerix™B[7]

End point description:

Anti-hepatitis B (Hep B) antibodies were measured by VITROS ECi/ECiQ Immunodiagnostic System using chemiluminescence detection technology. Subjects vaccinated in Study A3L15 were assessed at Year 1 (Visit 01) defined as the first time point of follow-up at about 2 years (Month [M] 24 to M27) post-booster vaccination, when subjects were aged 3.5 years and also at Year 2 (Visit 02) defined as the second time point of follow-up at about 3 years (M36 to M39) post-booster vaccination, when subjects were aged 4.5 years.

End point type	Primary

End point timeframe:

Month 24 to Month 27 and Month 36 to Month 39 post-booster dose

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	173	177	103	
Units: Percentage of subjects				
number (not applicable)				
Anti-Hep B; A3L15 Primary (D126; ≥10 mIU/mL)	95.2	95.5	98.8	
Anti-Hep B; A3L15 Primary (D126; ≥100 mIU/mL)	75.2	63.1	96.3	
Anti-Hep B; A3L15 Pre-Booster (D540; ≥10 mIU/mL)	76.9	92	93	
Anti-Hep B; A3L15 Pre-Booster (D540; ≥100 mIU/mL)	36.7	55.1	75	
Anti-Hep B; A3L15 Post-Booster (D570; ≥10 mIU/mL)	98.2	90	100	
Anti-Hep B; A3L15 Post-Booster (D570; ≥100 mIU/mL)	93.4	54.1	99	
Anti-Hep B; A3L26 Y1-V01 (M24 to M27; ≥10 mIU/mL)	76.3	72.7	96.1	
Anti-Hep B; A3L26 Y1-V01 (M24 to M27; ≥100 mIU/mL)	49.1	22.2	86.4	
Anti-Hep B; A3L26 Y2-V02 (M36 to M39; ≥10 mIU/mL)	73.3	68.5	96.1	
Anti-Hep B; A3L26 Y2-V02 (M36 to M39; ≥100 mIU/mL)	40	17	84.3	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Anti- PRP Immunogenicity Response at Primary Series Vaccination, at Age 3.5 Years and at Age 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T combined vaccine or CombAct-Hib™ and OPV and Engerix™ B.

End point title	Percentage of Subjects with Anti- PRP Immunogenicity Response at Primary Series Vaccination, at Age 3.5 Years and at Age 4.5 Years old after Primary Series Vaccinations with DTaP-IPV-Hep B-PRP-T combined vaccine or CombAct-Hib™ and OPV and Engerix™ B.[8]

End point description:

Anti-Haemophilus influenzae type b capsular polyribosyl ribitol phosphate (PRP) antibody concentrations were measured using a Farr-type radioimmunoassay (RIA). Subjects vaccinated in Study A3L15 were assessed at Year 1 (Visit 01) defined as the first time point of follow-up at about 2 years (Month [M] 24 to M27) post-booster vaccination, when subjects were aged 3.5 years and also at Year 2 (Visit 02) defined as the second time point of follow-up at about 3 years (M36 to M39) post-booster vaccination, when subjects were aged 4.5 years.

End point type	Primary

End point timeframe:

Month 24 to Month 27 and Month 36 to Month 39 post-booster dose

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	173	177	103	
Units: Percentage of subjects				
number (not applicable)				
Anti-PRP; A3L15 Primary (D126; ≥0.15 µg/mL)	95.9	100	98	
Anti-PRP; A3L15 Primary (D126; ≥1.0 µg/mL)	79.1	93.2	74.5	
Anti-PRP; A3L15 Pre-Booster (D540; ≥0.15 µg/mL)	82.7	92.6	74.8	
Anti-PRP; A3L15 Pre-Booster (D540; ≥1.0 µg/mL)	45.1	54.9	35	
Anti-PRP; A3L15 Post-Booster (D570; ≥0.15 µg/mL)	100	100	100	
Anti-PRP; A3L15 Post-Booster (D570; ≥1.0 µg/mL)	98.8	98.9	100	
Anti-PRP; A3L26 Y1-V01 (M24 to M27; ≥0.15 µg/ml)	98.3	99.4	99	
Anti-PRP; A3L26 Y1-V01 (M24 to M27; ≥1.0 µg/ml)	87.9	87	89.3	
Anti-PRP; A3L26 Y2-V02 (M36 to M39; ≥0.15 µg/ml)	98.8	98.8	100	
Anti-PRP; A3L26 Y2-V02 (M36 to M39; ≥1.0 µg/ml)	84.7	84.1	78.4	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: No safety data were collected in A3L26.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	9.0

Frequency threshold for reporting non-serious adverse events: 5 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Safety data were not solicited or collected for this study.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 April 2010	Deletion of analysis of antibody titers of poliovirus from all sections of the protocol and updated reason for excluding the analysis of antibody titers of poliovirus.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported