Clinical trial results:
A phase III, randomised, controlled, single-blind study to evaluate the safety and immunogenicity of GlaxoSmithKline (GSK) Biologicals' HPV-16/18 L1 VLP AS04 vaccine administered according to a 2-dose schedule (0, 6 month) in 4-6 years old healthy female children.

Summary

EudraCT number	2011-005604-15
Trial protocol	Outside EU/EEA
Global end of trial date	

Results information

Result version number	v1
This version publication date	01 April 2017
First version publication date	01 April 2017

Trial information

Trial identification

Sponsor protocol code	115887

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01627561
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	Interim
Date of interim/final analysis	08 October 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

Safety:
To assess the safety, tolerability and occurrence of clinically relevant abnormalities in biochemistry and haematology parameters after administration of the HPV-16/18 L1 VLP AS04 vaccine according to a 2-dose schedule at 0, 6 months in 4-6 year old females, up to one month after the last dose (Month 7).
Immunogenicity:
To evaluate the immunogenicity (as determined by ELISA) of the HPV-16/18 L1 VLP AS04 vaccine administered according to a 2-dose schedule at 0, 6 months in 4-6 year old females , one month after the last dose (Month 7).

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2012
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	Colombia: 26
Country: Number of subjects enrolled	Mexico: 25
Country: Number of subjects enrolled	Panama: 97
Worldwide total number of subjects	148
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)	148

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:

Out of the 149 subjects who were enrolled for the study, only 148 were registered, hence 148 started the study.

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Pre-assignment period milestones

Number of subjects started	149[1]
Number of subjects completed	148

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Not registered: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of the 149 subjects who were enrolled for the study, only 148 were registered, hence 148 started the study

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

The study was single-blind until the Month 12 visit, then the study was open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cervarix Group

Arm description:

Subjects aged 4-6 years receiving 2 doses of Cervarix vaccine at Day 0 and Month 6

Arm type	Experimental
Investigational medicinal product name	Cervarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses administered intramuscularly in the deltoid muscle of the left arm at Day 0 and Month 6

Arm title	Priorix + Infanrix Group

Arm description:

Subjects aged 4-6 years receiving 1 dose of Priorix vaccine at Day 0 and 1 dose of Infanrix vaccine at Month 6

Arm type	Active comparator

Investigational medicinal product name	Priorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly in the deltoid muscle of the left/right arm at Day 0

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

Dosage and administration details:

1 dose administered intramuscularly in the deltoid muscle of the left/right arm at Month 6

Number of subjects in period 1	Cervarix Group	Priorix + Infanrix Group
Started	74	74
Completed	74	71
Not completed	0	3
Consent withdrawn by subject	-	2
Migrated/moved from study area	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix Group
Reporting group description:	
Subjects aged 4-6 years receiving 2 doses of Cervarix vaccine at Day 0 and Month 6	
Reporting group title	Priorix + Infanrix Group
Reporting group description:	
Subjects aged 4-6 years receiving 1 dose of Priorix vaccine at Day 0 and 1 dose of Infanrix vaccine at Month 6	

Reporting group values	Cervarix Group	Priorix + Infanrix Group	Total
Number of subjects	74	74	148
Age categorical Units: Subjects			

Age continuous			
Age continuous description			
Units: years			
arithmetic mean	4.3	4.4	
standard deviation	± 0.48	± 0.52	-
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	74	74	148
Male	0	0	0

End points

End points reporting groups

Reporting group title	Cervarix Group
Reporting group description:	
Subjects aged 4-6 years receiving 2 doses of Cervarix vaccine at Day 0 and Month 6	
Reporting group title	Priorix + Infanrix Group
Reporting group description:	
Subjects aged 4-6 years receiving 1 dose of Priorix vaccine at Day 0 and 1 dose of Infanrix vaccine at Month 6	

Primary: Number of subjects with any, Grade 3 and related solicited local symptoms.

End point title	Number of subjects with any, Grade 3 and related solicited local symptoms.[1]
End point description:	
Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) of injection site. Relationship analysis was not performed.	
End point type	Primary
End point timeframe:	
During the 7-day period (Days 0-6) following each vaccination	

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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects				
Any Pain Dose 1 (N=74,74)	45	15		
Grade 3 Pain Dose 1 (N=74,74)	2	0		
Any Redness Dose 1 (N=74,74)	10	7		
Grade 3 Redness Dose 1 (N=74,74)	1	0		
Any Swelling Dose 1 (N=74,74)	6	6		
Grade 3 Swelling Dose 1 (N=74,74)	1	0		
Any Pain Dose 2 (N=72,71)	43	36		
Grade 3 Pain Dose 2 (N=72,71)	2	1		
Any Redness Dose 2 (N=72,71)	12	12		
Grade 3 Redness Dose 2 (N=72,71)	0	4		
Any Swelling Dose 2 (N=72,71)	16	15		
Grade 3 Swelling Dose 2 (N=72,71)	3	7		
Any Pain Across doses (N=74,74)	54	40		
Grade 3 Pain Across doses (N=74,74)	4	1		
Any Redness Across doses (N=74,74)	18	18		
Grade 3 Redness Across doses (N=74,74)	1	4		
Any Swelling Across doses (N=74,74)	19	18		

Grade 3 Swelling Across doses (N=74,74)	4	7		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any, Grade 3 and related solicited general symptoms.

End point title	Number of subjects with any, Grade 3 and related solicited general symptoms.[2]

End point description:

Assessed solicited general symptoms were arthralgia, fatigue, fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)], headache, myalgia, shivering and sweating. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.0 °C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Primary

End point timeframe:

During the 7-day period (Days 0-6) following each vaccination

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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects				
Any Arthralgia Dose 1 (N=74,74)	5	8		
Grade 3 Arthralgia Dose 1 (N=74,74)	0	0		
Related Arthralgia Dose 1 (N=74,74)	4	8		
Any Drowsiness Dose 1 (N=74,74)	14	7		
Grade 3 Drowsiness Dose 1 (N=74,74)	3	0		
Related Drowsiness Dose 1 (N=74,74)	12	7		
Any Fatigue Dose 1 (N=74,74)	8	7		
Grade 3 Fatigue Dose 1 (N=74,74)	0	0		
Related Fatigue Dose 1 (N=74,74)	7	7		
Any Fever Dose 1 (N=74,74)	6	8		
Grade 3 Fever Dose 1 (N=74,74)	1	0		
Related Fever Dose 1 (N=74,74)	3	5		
Any Gastrointestinal Dose 1 (N=74,74)	7	12		
Grade 3 Gastrointestinal Dose 1 (N=74,74)	0	0		
Related Gastrointestinal Dose 1 (N=74,74)	5	10		
Any Headache Dose 1 (N=74,74)	11	19		
Grade 3 Headache Dose 1 (N=74,74)	0	1		
Related Headache Dose 1 (N=74,74)	9	16		
Any Irritability Dose 1 (N=74,74)	13	7		

Grade 3 Irritability Dose 1 (N=74,74)	1	0		
Related Irritability Dose 1 (N=74,74)	12	7		
Any Loss of appetite Dose 1 (N=74,74)	15	7		
Grade 3 Loss of appetite Dose 1 (N=74,74)	0	0		
Related Loss of appetite Dose 1 (N=74,74)	13	7		
Any Myalgia Dose 1 (N=74,74)	13	9		
Grade 3 Myalgia Dose 1 (N=74,74)	0	0		
Related Myalgia Dose 1 (N=74,74)	13	9		
Any Rash Dose 1 (N=74,74)	3	1		
Grade 3 Rash Dose 1 (N=74,74)	0	0		
Related Rash Dose 1 (N=74,74)	2	1		
Any Urticaria Dose 1 (N=74,74)	5	3		
Grade 3 Urticaria Dose 1 (N=74,74)	0	0		
Related Urticaria Dose 1 (N=74,74)	4	2		
Any Arthralgia Dose 2 (N=72,71)	10	8		
Grade 3 Arthralgia Dose 2 (N=72,71)	0	0		
Related Arthralgia Dose 2 (N=72,71)	9	8		
Any Drowsiness Dose 2 (N=72,71)	9	9		
Grade 3 Drowsiness Dose 2 (N=72,71)	0	0		
Related Drowsiness Dose 2 (N=72,71)	9	9		
Any Fatigue Dose 2 (N=72,71)	9	7		
Grade 3 Fatigue Dose 2 (N=72,71)	0	0		
Related Fatigue Dose 2 (N=72,71)	8	7		
Any Fever Dose 2 (N=72,71)	7	12		
Grade 3 Fever Dose 2 (N=72,71)	0	0		
Related Fever Dose 2 (N=72,71)	6	9		
Any Gastrointestinal Dose 2 (N=72,71)	4	9		
Grade 3 Gastrointestinal Dose 2 (N=72,71)	0	0		
Related Gastrointestinal Dose 2 (N=72,71)	2	8		
Any Headache Dose 2 (N=72,71)	12	13		
Grade 3 Headache Dose 2 (N=72,71)	0	0		
Related Headache Dose 2 (N=72,71)	12	12		
Any Irritability Dose 2 (N=72,71)	18	17		
Grade 3 Irritability Dose 2 (N=72,71)	0	0		
Related Irritability Dose 2 (N=72,71)	18	17		
Any Loss of appetite Dose 2 (N=72,71)	9	8		
Grade 3 Loss of appetite Dose 2 (N=72,71)	1	1		
Related Loss of appetite Dose 2 (N=72,71)	8	8		
Any Myalgia Dose 2 (N=72,71)	13	11		
Grade 3 Myalgia Dose 2 (N=72,71)	0	0		
Related Myalgia Dose 2 (N=72,71)	12	11		
Any Rash Dose 2 (N=72,71)	3	4		
Grade 3 Rash Dose 2 (N=72,71)	0	0		
Related Rash Dose 2 (N=72,71)	3	3		
Any Urticaria Dose 2 (N=72,71)	5	4		
Grade 3 Urticaria Dose 2 (N=72,71)	0	0		
Related Urticaria Dose 2 (N=72,71)	4	3		
Any Arthralgia Across doses (N=74,74)	13	11		

Grade 3 Arthralgia Across doses (N=74,74)	0	0		
Related Arthralgia Across doses (N=74,74)	12	11		
Any Drowsiness Across doses (N=74,74)	16	15		
Grade 3 Drowsiness Across doses (N=74,74)	3	0		
Related Drowsiness Across doses (N=74,74)	15	15		
Any Fatigue Across doses (N=74,74)	15	10		
Grade 3 Fatigue Across doses (N=74,74)	0	0		
Related Fatigue Across doses (N=74,74)	13	10		
Any Fever Across doses (N=74,74)	12	17		
Grade 3 Fever Across doses (N=74,74)	1	0		
Related Fever Across doses (N=74,74)	8	13		
Any Gastrointestinal Across doses (N=74,74)	11	16		
Grade 3 Gastrointestinal Across doses (N=74,74)	0	0		
Related Gastrointestinal Across doses (N=74,74)	7	15		
Any Headache Across doses (N=74,74)	18	25		
Grade 3 Headache Across doses (N=74,74)	0	1		
Related Headache Across doses (N=74,74)	16	22		
Any Irritability Across doses (N=74,74)	22	19		
Grade 3 Irritability Across doses (N=74,74)	1	0		
Related Irritability Across doses (N=74,74)	22	19		
Any Loss of appetite Across doses (N=74,74)	21	13		
Grade 3 Loss of appetite Across doses (N=74,74)	1	1		
Related Loss of appetite Across doses (N=74,74)	18	13		
Any Myalgia Across doses (N=74,74)	21	14		
Grade 3 Myalgia Across doses (N=74,74)	0	0		
Related Myalgia Across doses (N=74,74)	21	14		
Any Rash Across doses (N=74,74)	6	5		
Grade 3 Rash Across doses (N=74,74)	0	0		
Related Rash Across doses (N=74,74)	5	4		
Any Urticaria Across doses (N=74,74)	10	7		
Grade 3 Urticaria Across doses (N=74,74)	0	0		
Related Urticaria Across doses (N=74,74)	8	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with unsolicited any, Grade 3 and related adverse events (AEs).

End point title	Number of subjects with unsolicited any, Grade 3 and related adverse events (AEs).[3]

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

End point type	Primary

End point timeframe:

During the 43-day period (Days 0-42) post vaccination Dose 1

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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects				
Any AEs	40	40		
Grade 3 AEs	3	2		
Related AEs	1	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with unsolicited any, Grade 3 and related adverse events (AEs).

End point title	Number of subjects with unsolicited any, Grade 3 and related adverse events (AEs).[4]

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

End point type	Primary

End point timeframe:

During the 30-day period (Days 0-29) post vaccination Dose 2 at Month 6

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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	71		
Units: Subjects				
Any AEs	18	13		
Grade 3 AEs	0	0		
Related AEs	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters.

End point title	Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters.[5]

End point description:

The parameters assessed were both biochemical (alanine aminotransferase = ALAT, creatinine = CREA, urea nitrogen = BUN) and haematological (basophils = BAS, eosinophils = EOS, red blood cells = RBC, hematocrit = HCT, hemoglobin, leukocytes [white blood cells] = WBC, lymphocytes, monocytes, neutrophils and platelets). Results were split into 2 outcomes due to the table size. Note that "99999"is a placeholder value since the number of subjects the respective categories was 0, hence the statistical analysis could not be performed.

End point type	Primary

End point timeframe:

42 days post dose 1 (PRE) and at 30 days post dose 2 (POST)

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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	69		
Units: Subjects				
ALAT, PRE Unknown Unknown [N=2;2]	0	0		
ALAT, PRE Unknown Below [N=2;2]	0	0		
ALAT, PRE Unknown Within [N=2;2]	2	2		
ALAT, PRE Unknown Above [N=2;2]	0	0		
ALAT, PRE Below Unknown [N=2;1]	0	0		
ALAT, PRE Below Below [N=2;1]	1	0		
ALAT, PRE Below Within [N=2;1]	1	1		
ALAT, PRE Below Above [N=2;1]	0	0		
ALAT, PRE Within Unknown [N=67;64]	0	0		
ALAT, PRE Within Below [N=67;64]	0	0		
ALAT, PRE Within Within [N=67;64]	64	62		
ALAT, PRE Within Above [N=67;64]	3	2		
ALAT, PRE Above Unknown [N=3;5]	0	0		
ALAT, PRE Above Below [N=3;5]	0	0		
ALAT, PRE Above Within [N=3;5]	1	3		

ALAT, PRE Above Above [N=3;5]	2	2		
ALAT, POST Unknown Unknown [N=2;2]	0	0		
ALAT, POST Unknown Below [N=2;2]	0	0		
ALAT, POST Unknown Within [N=2;2]	2	2		
ALAT, POST Unknown Above [N=2;2]	0	0		
ALAT, POST Below Unknown [N=2;1]	0	0		
ALAT, POST Below Below [N=2;1]	1	0		
ALAT, POST Below Within [N=2;1]	1	1		
ALAT, POST Below Above [N=2;1]	0	0		
ALAT, POST Within Unknown [N=66;64]	0	0		
ALAT, POST Within Below [N=66;64]	2	2		
ALAT, POST Within Within [N=66;64]	64	61		
ALAT, POST Within Above [N=66;64]	0	1		
ALAT, POST Above Unknown [N=3;5]	0	0		
ALAT, POST Above Below [N=3;5]	0	0		
ALAT, POST Above Within [N=3;5]	2	5		
ALAT, POST Above Above [N=3;5]	1	0		
BAS, PRE Unknown Unknown [N=2;0]	0	99999		
BAS, PRE Unknown Below [N=2;0]	0	99999		
BAS, PRE Unknown Within [N=2;0]	2	99999		
BAS, PRE Unknown Above [N=2;0]	0	99999		
BAS, PRE Below Unknown [N=0;0]	99999	99999		
BAS, PRE Below Below [N=0;0]	99999	99999		
BAS, PRE Below Within [N=0;0]	99999	99999		
BAS, PRE Below Above [N=0;0]	99999	99999		
BAS, PRE Within Unknown [N=70;69]	0	0		
BAS, PRE Within Below [N=70;69]	0	0		
BAS, PRE Within Within [N=70;69]	70	69		
BAS, PRE Within Above [N=70;69]	0	0		
BAS, PRE Above Unknown [N=0;4]	99999	0		
BAS, PRE Above Below [N=0;4]	99999	0		
BAS, PRE Above Within [N=0;4]	99999	4		
BAS, PRE Above Above [N=0;4]	99999	0		
BAS, POST Unknown Unknown [N=2;0]	0	99999		
BAS, POST Unknown Below [N=2;0]	0	99999		
BAS, POST Unknown Within [N=2;0]	2	99999		
BAS, POST Unknown Above [N=2;0]	0	99999		
BAS, POST Below Unknown [N=0;0]	99999	99999		
BAS, POST Below Below [N=0;0]	99999	99999		
BAS, POST Below Within [N=0;0]	99999	99999		
BAS, POST Below Above [N=0;0]	99999	99999		
BAS, POST Within Unknown [N=72;68]	0	0		
BAS, POST Within Below [N=72;68]	0	0		
BAS, POST Within Within [N=72;68]	71	67		
BAS, POST Within Above [N=72;68]	1	1		
BAS, POST Above Unknown [N=0;4]	99999	0		
BAS, POST Above Below [N=0;4]	99999	0		
BAS, POST Above Within [N=0;4]	99999	2		
BAS, POST Above Above [N=0;4]	99999	2		
CREA, PRE Unknown Unknown [N=2;1]	0	0		
CREA, PRE Unknown Below [N=2;1]	0	0		
CREA, PRE Unknown Within [N=2;1]	2	1		

CREA, PRE Unknown Above [N=2;1]	0	0		
CREA, PRE Below Unknown [N=27;22]	0	0		
CREA, PRE Below Below [N=27;22]	20	15		
CREA, PRE Below Within [N=27;22]	7	7		
CREA, PRE Below Above [N=27;22]	0	0		
CREA, PRE Within Unknown [N=45;49]	0	1		
CREA, PRE Within Below [N=45;49]	7	12		
CREA, PRE Within Within [N=45;49]	38	36		
CREA, PRE Within Above [N=45;49]	0	0		
CREA, PRE Above Unknown [N=0;1]	99999	0		
CREA, PRE Above Below [N=0;1]	99999	0		
CREA, PRE Above Within [N=0;1]	99999	1		
CREA, PRE Above Above [N=0;1]	99999	0		
CREA, POST Unknown Unknown [N=2;1]	0	0		
CREA, POST Unknown Below [N=2;1]	1	0		
CREA, POST Unknown Within [N=2;1]	1	1		
CREA, POST Unknown Above [N=2;1]	0	0		
CREA, POST Below Unknown [N=26;22]	0	0		
CREA, POST Below Below [N=26;22]	20	18		
CREA, POST Below Within [N=26;22]	6	4		
CREA, POST Below Above [N=26;22]	0	0		
CREA, POST Within Unknown [N=45;48]	0	1		
CREA, POST Within Below [N=45;48]	11	11		
CREA, POST Within Within [N=45;48]	34	36		
CREA, POST Within Above [N=45;48]	0	0		
CREA, POST Above Unknown [N=0;1]	99999	0		
CREA, POST Above Below [N=0;1]	99999	1		
CREA, POST Above Within [N=0;1]	99999	0		
CREA, POST Above Above [N=0;1]	99999	0		
EOS, PRE Unknown Unknown [N=2;0]	0	99999		
EOS, PRE Unknown Below [N=2;0]	0	99999		
EOS, PRE Unknown Within [N=2;0]	2	99999		
EOS, PRE Unknown Above [N=2;0]	0	99999		
EOS, PRE Below Unknown [N=1;0]	0	99999		
EOS, PRE Below Below [N=1;0]	0	99999		
EOS, PRE Below Within [N=1;0]	1	99999		
EOS, PRE Below Above [N=1;0]	0	99999		
EOS, PRE Within Unknown [N=49;50]	0	0		
EOS, PRE Within Below [N=49;50]	1	1		
EOS, PRE Within Within [N=49;50]	41	38		
EOS, PRE Within Above [N=49;50]	7	11		
EOS, PRE Above Unknown [N=20;23]	0	0		
EOS, PRE Above Below [N=20;23]	0	1		
EOS, PRE Above Within [N=20;23]	3	10		
EOS, PRE Above Above [N=20;23]	17	12		
EOS, POST Unknown Unknown [N=2;0]	0	99999		
EOS, POST Unknown Below [N=2;0]	0	99999		
EOS, POST Unknown Within [N=2;0]	2	99999		
EOS, POST Unknown Above [N=2;0]	0	99999		
EOS, POST Below Unknown [N=1;0]	0	99999		
EOS, POST Below Below [N=1;0]	0	99999		

EOS, POST Below Within [N=1;0]	1	99999		
EOS, POST Below Above [N=1;0]	0	99999		
EOS, POST Within Unknown [N=51;49]	0	0		
EOS, POST Within Below [N=51;49]	0	1		
EOS, POST Within Within [N=51;49]	42	35		
EOS, POST Within Above [N=51;49]	9	13		
EOS, POST Above Unknown [N=20;23]	0	0		
EOS, POST Above Below [N=20;23]	0	0		
EOS, POST Above Within [N=20;23]	2	10		
EOS, POST Above Above [N=20;23]	18	13		
RBC, PRE Unknown Unknown [N=2;0]	0	99999		
RBC, PRE Unknown Below [N=2;0]	0	99999		
RBC, PRE Unknown Within [N=2;0]	2	99999		
RBC, PRE Unknown Above [N=2;0]	0	99999		
RBC, PRE Below Unknown [N=4;4]	0	0		
RBC, PRE Below Below [N=4;4]	0	0		
RBC, PRE Below Within [N=4;4]	4	4		
RBC, PRE Below Above [N=4;4]	0	0		
RBC, PRE Within Unknown [N=66;66]	0	0		
RBC, PRE Within Below [N=66;66]	3	2		
RBC, PRE Within Within [N=66;66]	61	63		
RBC, PRE Within Above [N=66;66]	2	1		
RBC, PRE Above Unknown [N=0;3]	99999	0		
RBC, PRE Above Below [N=0;3]	99999	0		
RBC, PRE Above Within [N=0;3]	99999	2		
RBC, PRE Above Above [N=0;3]	99999	1		
RBC, POST Unknown Unknown [N=2;0]	0	99999		
RBC, POST Unknown Below [N=2;0]	0	99999		
RBC, POST Unknown Within [N=2;0]	2	99999		
RBC, POST Unknown Above [N=2;0]	0	99999		
RBC, POST Below Unknown [N=4;4]	0	0		
RBC, POST Below Below [N=4;4]	0	2		
RBC, POST Below Within [N=4;4]	4	2		
RBC, POST Below Above [N=4;4]	0	0		
RBC, POST Within Unknown [N=68;65]	0	0		
RBC, POST Within Below [N=68;65]	2	2		
RBC, POST Within Within [N=68;65]	65	63		
RBC, POST Within Above [N=68;65]	1	0		
RBC, POST Above Unknown [N=0;3]	99999	0		
RBC, POST Above Below [N=0;3]	99999	0		
RBC, POST Above Within [N=0;3]	99999	2		
RBC, POST Above Above [N=0;3]	99999	1		
HCT, PRE Unknown Unknown [N=2;0]	0	99999		
HCT, PRE Unknown Below [N=2;0]	0	99999		
HCT, PRE Unknown Within [N=2;0]	2	99999		
HCT, PRE Unknown Above [N=2;0]	0	99999		
HCT, PRE Below Unknown [N=19;21]	0	0		
HCT, PRE Below Below [N=19;21]	8	12		
HCT, PRE Below Within [N=19;21]	11	8		
HCT, PRE Below Above [N=19;21]	0	1		
HCT, PRE Within Unknown [N=48;48]	0	0		
HCT, PRE Within Below [N=48;48]	5	1		

HCT, PRE Within Within [N=48;48]	41	42		
HCT, PRE Within Above [N=48;48]	2	5		
HCT, PRE Above Unknown [N=3;4]	0	0		
HCT, PRE Above Below [N=3;4]	0	0		
HCT, PRE Above Within [N=3;4]	2	4		
HCT, PRE Above Above [N=3;4]	1	0		
HCT, POST Unknown Unknown [N=2;0]	0	99999		
HCT, POST Unknown Below [N=2;0]	0	99999		
HCT, POST Unknown Within [N=2;0]	1	99999		
HCT, POST Unknown Above [N=2;0]	1	99999		
HCT, POST Below Unknown [N=20;21]	0	0		
HCT, POST Below Below [N=20;21]	5	10		
HCT, POST Below Within [N=20;21]	15	11		
HCT, POST Below Above [N=20;21]	0	0		
HCT, POST Within Unknown [N=49;47]	0	0		
HCT, POST Within Below [N=49;47]	3	3		
HCT, POST Within Within [N=49;47]	45	44		
HCT, POST Within Above [N=49;47]	1	0		
HCT, POST Above Unknown [N=3;4]	0	0		
HCT, POST Above Below [N=3;4]	0	0		
HCT, POST Above Within [N=3;4]	3	4		
HCT, POST Above Above [N=3;4]	0	0		
Hemoglobin, PRE Unknown Unknown [N=2;0]	0	99999		
Hemoglobin, PRE Unknown Below [N=2;0]	0	99999		
Hemoglobin, PRE Unknown Within [N=2;0]	1	99999		
Hemoglobin, PRE Unknown Above [N=2;0]	1	99999		
Hemoglobin, PRE Below Unknown [N=15;11]	0	0		
Hemoglobin, PRE Below Below [N=15;11]	7	2		
Hemoglobin, PRE Below Within [N=15;11]	8	9		
Hemoglobin, PRE Below Above [N=15;11]	0	0		
Hemoglobin, PRE Within Unknown [N=50;56]	0	0		
Hemoglobin, PRE Within Below [N=50;56]	3	6		
Hemoglobin, PRE Within Within [N=50;56]	43	46		
Hemoglobin, PRE Within Above [N=50;56]	4	4		
Hemoglobin, PRE Above Unknown [N=5;6]	0	0		
Hemoglobin, PRE Above Below [N=5;6]	0	0		
Hemoglobin, PRE Above Within [N=5;6]	3	5		
Hemoglobin, PRE Above Above [N=5;6]	2	1		
Hemoglobin, POST Unknown Unknown [N=2;0]	0	99999		
Hemoglobin, POST Unknown Below [N=2;0]	0	99999		
Hemoglobin, POST Unknown Within [N=2;0]	1	99999		

Hemoglobin, POST Unknown Above [N=2;0]	1	99999		
Hemoglobin, POST Below Unknown [N=16;11]	0	0		
Hemoglobin, POST Below Below [N=16;11]	1	2		
Hemoglobin, POST Below Within [N=16;11]	15	9		
Hemoglobin, POST Below Above [N=16;11]	0	0		
Hemoglobin, POST Within Unknown [N=51;55]	0	0		
Hemoglobin, POST Within Below [N=51;55]	1	4		
Hemoglobin, POST Within Within [N=51;55]	44	50		
Hemoglobin, POST Within Above [N=51;55]	6	1		
Hemoglobin, POST Above Unknown [N=5;6]	0	0		
Hemoglobin, POST Above Below [N=5;6]	0	0		
Hemoglobin, POST Above Within [N=5;6]	3	5		
Hemoglobin, POST Above Above [N=5;6]	2	1		
WBC, PRE Unknown Unknown [N=2;0]	0	99999		
WBC, PRE Unknown Below [N=2;0]	0	99999		
WBC, PRE Unknown Within [N=2;0]	1	99999		
WBC, PRE Unknown Above [N=2;0]	1	99999		
WBC, PRE Below Unknown [N=5;7]	0	0		
WBC, PRE Below Below [N=5;7]	1	5		
WBC, PRE Below Within [N=5;7]	3	1		
WBC, PRE Below Above [N=5;7]	1	1		
WBC, PRE Within Unknown [N=62;61]	0	0		
WBC, PRE Within Below [N=62;61]	3	1		
WBC, PRE Within Within [N=62;61]	56	57		
WBC, PRE Within Above [N=62;61]	3	3		
WBC, PRE Above Unknown [N=3;5]	0	0		
WBC, PRE Above Below [N=3;5]	0	0		
WBC, PRE Above Within [N=3;5]	1	3		
WBC, PRE Above Above [N=3;5]	2	2		
WBC, POST Unknown Unknown [N=2;0]	0	99999		
WBC, POST Unknown Below [N=2;0]	0	99999		
WBC, POST Unknown Within [N=2;0]	2	99999		
WBC, POST Unknown Above [N=2;0]	0	99999		
WBC, POST Below Unknown [N=5;7]	0	0		
WBC, POST Below Below [N=5;7]	3	4		
WBC, POST Below Within [N=5;7]	2	3		
WBC, POST Below Above [N=5;7]	0	0		
WBC, POST Within Unknown [N=63;60]	0	0		
WBC, POST Within Below [N=63;60]	1	7		
WBC, POST Within Within [N=63;60]	60	50		
WBC, POST Within Above [N=63;60]	2	3		
WBC, POST Above Unknown [N=4;5]	0	0		
WBC, POST Above Below [N=4;5]	0	0		

WBC, POST Above Within [N=4;5]	2	4		
WBC, POST Above Above [N=4;5]	2	1		
Lymphocytes, PRE Unknown Unknown [N=2;0]	0	99999		
Lymphocytes, PRE Unknown Below [N=2;0]	0	99999		
Lymphocytes, PRE Unknown Within [N=2;0]	1	99999		
Lymphocytes, PRE Unknown Above [N=2;0]	1	99999		
Lymphocytes, PRE Below Unknown [N=7;10]	0	0		
Lymphocytes, PRE Below Below [N=7;10]	4	6		
Lymphocytes, PRE Below Within [N=7;10]	2	2		
Lymphocytes, PRE Below Above [N=7;10]	1	2		
Lymphocytes, PRE Within Unknown [N=48;42]	0	0		
Lymphocytes, PRE Within Below [N=48;42]	7	2		
Lymphocytes, PRE Within Within [N=48;42]	38	34		
Lymphocytes, PRE Within Above [N=48;42]	3	6		
Lymphocytes, PRE Above Unknown [N=15;21]	0	0		
Lymphocytes, PRE Above Below [N=15;21]	0	2		
Lymphocytes, PRE Above Within [N=15;21]	6	5		
Lymphocytes, PRE Above Above [N=15;21]	9	14		
Lymphocytes, POST Unknown Unknown [N=2;0]	0	99999		
Lymphocytes, POST Unknown Below [N=2;0]	0	99999		
Lymphocytes, POST Unknown Within [N=2;0]	2	99999		
Lymphocytes, POST Unknown Above [N=2;0]	0	99999		
Lymphocytes, POST Below Unknown [N=7;10]	0	0		
Lymphocytes, POST Below Below [N=7;10]	6	6		
Lymphocytes, POST Below Within [N=7;10]	1	4		
Lymphocytes, POST Below Above [N=7;10]	0	0		
Lymphocytes, POST Within Unknown [N=49;42]	0	0		
Lymphocytes, POST Within Below [N=49;42]	6	5		
Lymphocytes, POST Within Within [N=49;42]	38	37		
Lymphocytes, POST Within Above [N=49;42]	5	0		
Lymphocytes, POST Above Unknown [N=16;20]	0	0		
Lymphocytes, POST Above Below [N=16;20]	0	1		

Lymphocytes, POST Above Within [N=16;20]	16	15		
Lymphocytes, POST Above Above [N=16;20]	0	4		
Monocytes, PRE Unknown Unknown [N=2;0]	0	99999		
Monocytes, PRE Unknown Below [N=2;0]	1	99999		
Monocytes, PRE Unknown Within [N=2;0]	1	99999		
Monocytes, PRE Unknown Above [N=2;0]	0	99999		
Monocytes, PRE Below Unknown [N=7;9]	0	0		
Monocytes, PRE Below Below [N=7;9]	4	5		
Monocytes, PRE Below Within [N=7;9]	3	4		
Monocytes, PRE Below Above [N=7;9]	0	0		
Monocytes, PRE Within Unknown [N=51;55]	0	0		
Monocytes, PRE Within Below [N=51;55]	3	2		
Monocytes, PRE Within Within [N=51;55]	42	48		
Monocytes, PRE Within Above [N=51;55]	6	5		
Monocytes, PRE Above Unknown [N=12;9]	0	0		
Monocytes, PRE Above Below [N=12;9]	0	0		
Monocytes, PRE Above Within [N=12;9]	6	3		
Monocytes, PRE Above Above [N=12;9]	6	6		
Monocytes, POST Unknown Unknown [N=2;0]	0	99999		
Monocytes, POST Unknown Below [N=2;0]	1	99999		
Monocytes, POST Unknown Within [N=2;0]	1	99999		
Monocytes, POST Unknown Above [N=2;0]	0	99999		
Monocytes, POST Below Unknown [N=7;9]	0	0		
Monocytes, POST Below Below [N=7;9]	2	4		
Monocytes, POST Below Within [N=7;9]	5	4		
Monocytes, POST Below Above [N=7;9]	0	1		
Monocytes, POST Within Unknown [N=53;54]	0	0		
Monocytes, POST Within Below [N=53;54]	4	3		
Monocytes, POST Within Within [N=53;54]	49	51		
Monocytes, POST Within Above [N=53;54]	0	0		
Monocytes, POST Above Unknown [N=12;9]	0	0		
Monocytes, POST Above Below [N=12;9]	0	0		
Monocytes, POST Above Within [N=12;9]	12	7		
Monocytes, POST Above Above [N=12;9]	0	2		

Neutrophils, PRE Unknown Unknown [N=2;0]	0	99999		
Neutrophils, PRE Unknown Below [N=2;0]	1	99999		
Neutrophils, PRE Unknown Within [N=2;0]	1	99999		
Neutrophils, PRE Unknown Above [N=2;0]	0	99999		
Neutrophils, PRE Below Unknown [N=14;21]	0	0		
Neutrophils, PRE Below Below [N=14;21]	8	14		
Neutrophils, PRE Below Within [N=14;21]	6	6		
Neutrophils, PRE Below Above [N=14;21]	0	1		
Neutrophils, PRE Within Unknown [N=52;46]	0	0		
Neutrophils, PRE Within Below [N=52;46]	4	6		
Neutrophils, PRE Within Within [N=52;46]	41	39		
Neutrophils, PRE Within Above [N=52;46]	7	1		
Neutrophils, PRE Above Unknown [N=4;6]	0	0		
Neutrophils, PRE Above Below [N=4;6]	0	0		
Neutrophils, PRE Above Within [N=4;6]	3	3		
Neutrophils, PRE Above Above [N=4;6]	1	3		
Neutrophils, POST Unknown Unknown [N=2;0]	0	99999		
Neutrophils, POST Unknown Below [N=2;0]	0	99999		
Neutrophils, POST Unknown Within [N=2;0]	2	99999		
Neutrophils, POST Unknown Above [N=2;0]	0	99999		
Neutrophils, POST Below Unknown [N=15;21]	0	0		
Neutrophils, POST Below Below [N=15;21]	1	4		
Neutrophils, POST Below Within [N=15;21]	13	16		
Neutrophils, POST Below Above [N=15;21]	1	1		
Neutrophils, POST Within Unknown [N=53;45]	0	0		
Neutrophils, POST Within Below [N=53;45]	4	4		
Neutrophils, POST Within Within [N=53;45]	43	35		
Neutrophils, POST Within Above [N=53;45]	6	6		
Neutrophils, POST Above Unknown [N=4;6]	0	0		
Neutrophils, POST Above Below [N=4;6]	0	0		
Neutrophils, POST Above Within [N=4;6]	2	3		
Neutrophils, POST Above Above [N=4;6]	2	3		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters

End point title	Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters[6]

End point description:

The parameters assessed were both biochemical (alanine aminotransferase = ALAT, creatinine = CREA, urea nitrogen = BUN) and haematological (basophils = BAS, eosinophils = EOS, red blood cells = RBC, hematocrit = HCT, hemoglobin, leukocytes [white blood cells] = WBC, lymphocytes, monocytes, neutrophils and platelets). Results were split into 2 outcomes due to the table size. Note that "99999"is a placeholder value since the number of subjects the respective categories was 0, hence the statistical analysis could not be performed.

End point type	Primary

End point timeframe:

42 days post dose 1 (PRE) and at 30 days post dose 2 (POST)

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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	64		
Units: Subjects				
Platelets, PRE Unknown Unknown [N=3;0]	0	99999		
Platelets, PRE Unknown Below [N=3;0]	0	99999		
Platelets, PRE Unknown Within [N=3;0]	2	99999		
Platelets, PRE Unknown Above [N=3;0]	1	99999		
Platelets, PRE Below Unknown [N=0;2]	99999	0		
Platelets, PRE Below Below [N=0;2]	99999	0		
Platelets, PRE Below Within [N=0;2]	99999	2		
Platelets, PRE Below Above [N=0;2]	99999	0		
Platelets, PRE Within Unknown [N=60;58]	0	0		
Platelets, PRE Within Below [N=60;58]	0	0		
Platelets, PRE Within Within [N=60;58]	53	54		
Platelets, PRE Within Above [N=60;58]	7	4		
Platelets, PRE Above Unknown [N=9;13]	0	0		
Platelets, PRE Above Below [N=9;13]	0	0		
Platelets, PRE Above Within [N=9;13]	3	8		
Platelets, PRE Above Above [N=9;13]	6	5		
Platelets, POST Unknown Unknown [N=3;0]	0	99999		
Platelets, POST Unknown Below [N=3;0]	0	99999		

Platelets, POST Unknown Within [N=3;0]	2	99999		
Platelets, POST Unknown Above [N=3;0]	1	99999		
Platelets, POST Below Unknown [N=0;2]	99999	0		
Platelets, POST Below Below [N=0;2]	99999	0		
Platelets, POST Below Within [N=0;2]	99999	2		
Platelets, POST Below Above [N=0;2]	99999	0		
Platelets, POST Within Unknown [N=61;57]	0	0		
Platelets, POST Within Below [N=61;57]	0	0		
Platelets, POST Within Within [N=61;57]	58	56		
Platelets, POST Within Above [N=61;57]	3	1		
Platelets, POST Above Unknown [N=10;13]	0	0		
Platelets, POST Above Below [N=10;13]	0	0		
Platelets, POST Above Within [N=10;13]	6	7		
Platelets, POST Above Above [N=10;13]	4	6		
BUN, PRE Unknown Unknown [N=2;1]	0	0		
BUN, PRE Unknown Below [N=2;1]	0	0		
BUN, PRE Unknown Within [N=2;1]	2	1		
BUN, PRE Unknown Above [N=2;1]	0	0		
BUN, PRE Below Unknown [N=12;4]	0	0		
BUN, PRE Below Below [N=12;4]	4	1		
BUN, PRE Below Within [N=12;4]	8	3		
BUN, PRE Below Above [N=12;4]	0	0		
BUN, PRE Within Unknown [N=57;64]	0	0		
BUN, PRE Within Below [N=57;64]	2	7		
BUN, PRE Within Within [N=57;64]	54	57		
BUN, PRE Within Above [N=57;64]	1	0		
BUN, PRE Above Unknown [N=3;4]	0	0		
BUN, PRE Above Below [N=3;4]	0	0		
BUN, PRE Above Within [N=3;4]	3	4		
BUN, PRE Above Above [N=3;4]	0	0		
BUN, POST Unknown Unknown [N=2;1]	0	0		
BUN, POST Unknown Below [N=2;1]	0	0		
BUN, POST Unknown Within [N=2;1]	2	1		
BUN, POST Unknown Above [N=2;1]	0	0		
BUN, POST Below Unknown [N=12;4]	0	0		
BUN, POST Below Below [N=12;4]	5	0		
BUN, POST Below Within [N=12;4]	7	4		
BUN, POST Below Above [N=12;4]	0	0		
BUN, POST Within Unknown [N=55;63]	0	0		
BUN, POST Within Below [N=55;63]	3	10		
BUN, POST Within Within [N=55;63]	52	53		
BUN, POST Within Above [N=55;63]	0	0		
BUN, POST Above Unknown [N=3;4]	0	0		
BUN, POST Above Below [N=3;4]	0	0		
BUN, POST Above Within [N=3;4]	3	4		
BUN, POST Above Above [N=3;4]	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)[7]

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Primary

End point timeframe:

From first vaccination to one month after the last vaccine dose (from Day 0 up to Month 7)

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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with AEs and SAEs leading to withdrawal

End point title	Number of subjects with AEs and SAEs leading to withdrawal[8]

End point description:

End point type	Primary

End point timeframe:

From first vaccination to one month after the last vaccine dose (from Day 0 up to Month 7)

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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with potential immune-mediated diseases (pIMDs)

End point title	Number of subjects with potential immune-mediated diseases (pIMDs)[9]

End point description:

Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology

End point type	Primary

End point timeframe:

From first vaccination to one month after the last vaccine dose (from Day 0 up to Month 7)

Notes:

[9] - 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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with medically significant conditions (MSCs)

End point title	Number of subjects with medically significant conditions (MSCs)[10]

End point description:

MSCs include AEs prompting emergency room or physician visits that are not related to common diseases or routine visits for physical examination or vaccination, or serious adverse events (SAEs) that are not related to common diseases. Common diseases include upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervico-vaginal yeast infections, menstrual cycle abnormalities and injury.

End point type	Primary

End point timeframe:

From first vaccination to one month after the last vaccine dose (from Day 0 up to Month 7)

Notes:

[10] - 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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects	38	28		

Statistical analyses

No statistical analyses for this end point

Primary: Number of serconverted subjects for anti-HPV-16/18

End point title	Number of serconverted subjects for anti-HPV-16/18[11]

End point description:

A seroconverted subject was defined as a vaccinated subject who had either a pre-vaccination titer <1:10 and a post-vaccination titer ≥1:40 or a pre-vaccination titer ≥1:10 and at least a four-fold increase in post-vaccination titer.

End point type	Primary

End point timeframe:

One month after the last dose of study vaccine (Month 7)

Notes:

[11] - 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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	44		
Units: Subjects				
HPV-16	65	1		
HPV-18	63	1		

Statistical analyses

No statistical analyses for this end point

Primary: Anti-HPV-16/18 antibody concentrations

End point title	Anti-HPV-16/18 antibody concentrations[12]

End point description:

Antibody concentrations were assessed by Enzyme-linked-Immunosorbent Assay (ELISA) and expressed as geometric mean titers (GMTs) in ELISA units per milliliter (EU/mL).

End point type	Primary

End point timeframe:

One month after the last dose of study vaccine (Month 7)

Notes:

[12] - 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: This analysis was descriptive, hence no statistical analyses are available.

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	45		
Units: EU/mL				
geometric mean (confidence interval 95%)				
HPV-16	19677.4 (16463.7 to 23518.4)	10.9 (8.9 to 13.4)		
HPV-18	10509.1 (8818.9 to 12523.2)	9.6 (8.4 to 11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted for anti-HPV-16/18 antibodies

End point title	Number of subjects seroconverted for anti-HPV-16/18 antibodies

End point description:

Seroconversion is defined as the appearance of antibodies (i.e. titre greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. Values for Month 7 were primary outcomes and presented as such. Values past month 7 were not available at the time of posting this record and will be added once validated results become available.

End point type	Secondary

End point timeframe:

At Day 0, Month 7 and Month 12

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	45		
Units: Subjects				
HPV-16, Day 0	0	1		
HPV-18, Day 0	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16/18 antibody concentrations

End point title	Anti-HPV-16/18 antibody concentrations

End point description:

Antibody concentrations were calculated as geometric mean concentrations (GMCs), assessed by ELISA for the respective groups and expressed as ELISA units per milliliter (EU/mL). Values for Month 7 were primary outcomes and presented as such. Values past month 7 were not available at the time of posting this record and will be added once validated results become available.

End point type	Secondary

End point timeframe:

At Day 0, Month 7 and Month 12

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	45		
Units: EU/mL				
geometric mean (confidence interval 95%)				
HPV-16, Day 0	9.5 (9.5 to 9.5)	10.3 (8.8 to 12.1)		
HPV-18, Day 0	9.2 (8.9 to 9.6)	9 (9 to 9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with potential immune-mediated diseases (pIMDs)

End point title	Number of subjects with potential immune-mediated diseases (pIMDs)

End point description:

Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology

End point type	Secondary

End point timeframe:

From first vaccination to 6 months after the last vaccine dose (from Day 0 up to Month 12)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with medically significant conditions (MSCs)

End point title	Number of subjects with medically significant conditions (MSCs)

End point description:

MSCs include AEs prompting emergency room or physician visits that are not related to common diseases or routine visits for physical examination or vaccination, or serious adverse events (SAEs) that are not related to common diseases. Common diseases include upper respiratory infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, cervico-vaginal yeast infections, menstrual cycle abnormalities and injury.

End point type	Secondary

End point timeframe:

From first vaccination to 6 months after the last vaccine dose (from Day 0 up to Month 12)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects	38	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

From first vaccination to 6 months after the last vaccine dose (from Day 0 up to Month 12)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting the intake of concomitant medication

End point title	Number of subjects reporting the intake of concomitant medication

End point description:

End point type	Secondary

End point timeframe:

During the 43-day period (Days 0-42) following vaccination on Day 0 and during the 30-day period (Days 0-29) following vaccination at Month 6

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects				
Any medication, Dose 1 (N=74,74)	43	36		
Any antipyretic, Dose 1 (N=74,74)	27	22		
Prophylactic antipyretic, Dose 1 (N=74,74)	0	0		
Any antibiotic, Dose 1 (N=74,74)	17	10		
Any medication, Dose 2 (N=74,71)	19	23		
Any antipyretic, Dose 2 (N=74,71)	10	8		
Prophylactic antipyretic, Dose 2 (N=74,71)	0	0		
Any antibiotic, Dose 2 (N=74,71)	6	6		
Any medication, Accross doses (N=74,74)	49	43		
Any antipyretic, Accross doses (N=74,74)	30	25		
Prophylactic antipyretic, Accross doses (N=74,74)	0	0		
Any antibiotic, Accross doses (N=74,74)	20	15		

Statistical analyses

No statistical analyses for this end point

Secondary: The number of subjects completing the vaccination schedule in all groups.

End point title	The number of subjects completing the vaccination schedule in all groups.

End point description:

End point type	Secondary

End point timeframe:

From first vaccination to the last vaccine dose (from Day 0 up to Month 6)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects				
Subjects receiving 1 dose	0	3		
Subjects receiving 2 doses	74	71		
Subjects receiving any dose	74	74		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with of AEs/SAEs leading to withdrawal

End point title	Number of subjects with of AEs/SAEs leading to withdrawal

End point description:

End point type	Secondary

End point timeframe:

From Day 0 to Month 12

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: The number of subjects with solicited fever, measles/rubella-like rash, parotid gland swelling and signs of meningism, including febrile convulsion

End point title	The number of subjects with solicited fever, measles/rubella-like rash, parotid gland swelling and signs of meningism, including febrile convulsion

End point description:

End point type	Secondary

End point timeframe:

During the 43-day period (Days 0-42) following vaccination on Day 0

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects				
Fever ≥37.5°C	30	26		
Fever >39.0°C	7	2		
Related Fever	6	7		
Any rash	1	1		
Rash with fever	0	0		
Grade 3 rash	0	0		
Related rash	1	1		
Any Parotid gland swelling	0	0		
Any Signs of Meningism	0	1		
Grade 3 Signs of Meningism	0	0		
Related Signs of Meningism	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 7-day (Days 0-6) post-each dose
Unsolicited adverse events: within the 30-day (Days 0-29) post-each dose
Serious adverse events: from Day 0 up to Month 12

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Cervarix Group

Reporting group description:

Subjects aged 4-6 years receiving 2 doses of Cervarix vaccine at Day 0 and Month 6

Reporting group title	Priorix + Infanrix Group

Reporting group description:

Subjects aged 4-6 years receiving 1 dose of Priorix vaccine at Day 0 and 1 dose of Infanrix vaccine at Month 6

Serious adverse events	Cervarix Group	Priorix + Infanrix Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 74 (1.35%)	2 / 74 (2.70%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 74 (1.35%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cervarix Group	Priorix + Infanrix Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 74 (72.97%)	40 / 74 (54.05%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	54 / 74 (72.97%)	40 / 74 (54.05%)	
occurrences (all)	54	40	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 74 (24.32%)	18 / 74 (24.32%)	
occurrences (all)	18	18	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 74 (25.68%)	18 / 74 (24.32%)	
occurrences (all)	19	18	
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 74 (17.57%)	11 / 74 (14.86%)	
occurrences (all)	13	11	
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 74 (21.62%)	15 / 74 (20.27%)	
occurrences (all)	16	15	
Fever/(Axillary)			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 74 (16.22%)	17 / 74 (22.97%)	
occurrences (all)	12	17	

Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 74 (20.27%)	10 / 74 (13.51%)	
occurrences (all)	15	10	
Gastrointestinal			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 74 (14.86%)	16 / 74 (21.62%)	
occurrences (all)	11	16	
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 74 (24.32%)	25 / 74 (33.78%)	
occurrences (all)	18	25	
Irritability / fussiness			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 74 (29.73%)	19 / 74 (25.68%)	
occurrences (all)	22	19	
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 74 (28.38%)	14 / 74 (18.92%)	
occurrences (all)	21	14	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 74 (28.38%)	13 / 74 (17.57%)	
occurrences (all)	21	13	
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 74 (8.11%)	5 / 74 (6.76%)	
occurrences (all)	6	5	
Urticaria			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 74 (13.51%)	7 / 74 (9.46%)	
occurrences (all)	10	7	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	21 / 74 (28.38%)	23 / 74 (31.08%)	
occurrences (all)	21	23	
Pharyngitis			
subjects affected / exposed	4 / 74 (5.41%)	3 / 74 (4.05%)	
occurrences (all)	4	3	
Gastroenteritis			
subjects affected / exposed	3 / 74 (4.05%)	5 / 74 (6.76%)	
occurrences (all)	3	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported