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	06 October 2016

Results information

Result version number	v2 (current)
This version publication date	30 April 2020
First version publication date	01 April 2017
Version creation reason	

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	Final
Date of interim/final analysis	02 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 April 2014
Global end of trial reached?	Yes
Global end of trial date	06 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To assess the safety, reactogenicity and occurrence of clinically relevant abnormalities in biochemistry and haematology parameters after administration of the HPV-16/18 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).
• To evaluate the immunogenicity (as determined by enzyme-linked immunosorbent assay [ELISA]) of the HPV-16/18 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 for at least 30 minutes, with appropriate medical treatment readily available in case of anaphylaxis. 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?	Yes

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:

This study was conducted by multiple investigators at 7 centers in Colombia, Mexico and Panama.

Pre-assignment

Screening details:

All 148 subjects enrolled in the study, received the study vaccination and were included in the Total Vaccinated cohort (TVC).

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 from Day 0 up to Month 12, then the study was open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cervarix Group

Arm description:

Healthy female subjects aged between, and including, 4 and 6 years, who received two doses of Cervarix vaccine at Day 0 and Month 6, administered intramuscularly in the deltoid muscle of the left upper arm.

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:

Healthy female subjects aged between, and including, 4 and 6 years, who received one dose of Priorix vaccine at Day 0 and one dose of Infanrix vaccine at Month 6, administered intramuscularly in the deltoid muscle of the left upper arm.

Arm type	Active comparator
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 arm at Month 6.

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 arm at Day 0.

Number of subjects in period 1	Cervarix Group	Priorix + Infanrix Group
Started	74	74
Completed	73	71
Not completed	1	3
Consent withdrawn by subject	-	1
Migrated/moved from study area	-	2
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix Group
Reporting group description:	
Healthy female subjects aged between, and including, 4 and 6 years, who received two doses of Cervarix vaccine at Day 0 and Month 6, administered intramuscularly in the deltoid muscle of the left upper arm.	
Reporting group title	Priorix + Infanrix Group
Reporting group description:	
Healthy female subjects aged between, and including, 4 and 6 years, who received one dose of Priorix vaccine at Day 0 and one dose of Infanrix vaccine at Month 6, administered intramuscularly in the deltoid muscle of the left upper arm.	

Reporting group values	Cervarix Group	Priorix + Infanrix Group	Total
Number of subjects	74	74	148
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)	74	74	148
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: years			
arithmetic mean	4.3	4.4	
standard deviation	± 0.5	± 0.5	-
Gender categorical Units: Subjects			
Female	74	74	148
Male	0	0	0
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American	4	2	6
White - Caucasian / European Heritage	2	4	6
Mixed origin	68	68	136

End points

End points reporting groups

Reporting group title	Cervarix Group
Reporting group description:	
Healthy female subjects aged between, and including, 4 and 6 years, who received two doses of Cervarix vaccine at Day 0 and Month 6, administered intramuscularly in the deltoid muscle of the left upper arm.	
Reporting group title	Priorix + Infanrix Group
Reporting group description:	
Healthy female subjects aged between, and including, 4 and 6 years, who received one dose of Priorix vaccine at Day 0 and one dose of Infanrix vaccine at Month 6, administered intramuscularly in the deltoid muscle of the left upper arm.	

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

End point title	Number of subjects with any and Grade 3 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 = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 20 millimeters (mm) of injection site.	
End point type	Primary
End point timeframe:	
During the 7-day follow-up period (i.e. from the day of vaccination up to 6 subsequent days) after each vaccine dose and across doses	

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 (only in joints which were distal from the injection site), drowsiness, fatigue, fever [defined as axillary temperature equal to or above 37.5 degrees Celsius (°C)], gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain), headache, irritability/fussiness, loss of appetite, myalgia, rash (not urticaria, not measels/rubella-like rash), urticaria. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.0 °C. Grade 3 irritability/fussines = crying that could not be comforted/prevented normal activty. Grade 3 loss of appetite = did not eat at all. Related = symptom assessed by the investigator as causally related to the study vaccination.

End point type	Primary

End point timeframe:

During the 7-day follow-up period (i.e. from the day of vaccination up to 6 subsequent days) after each vaccine dose and across doses

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	17		
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	3		
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)	9	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)	7	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)	3	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)	9	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)	14	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)	9	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)	8	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	23		
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)	19	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	6		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any, Grade 3 and related unsolicited adverse events (AEs) reported during the 43-day period following the vaccination at Day 0

End point title	Number of subjects with any, Grade 3 and related unsolicited adverse events (AEs) reported during the 43-day period following the vaccination at Day 0[3]

End point description:

An unsolicited AE is 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. An AE could therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also included failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse. 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 = AE assessed by the investigator as causally related to the study vaccination.

End point type	Primary

End point timeframe:

During the 43-day period (i.e. from the day of vaccination up to 42 subsequent days) following the vaccination at Day 0

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 AE(s)	40	40		
Grade 3 AE(s)	3	2		
Related AE(s)	1	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any, Grade 3 and related unsolicited AEs reported during the 30-day period following the vaccination at Month 6

End point title	Number of subjects with any, Grade 3 and related unsolicited AEs reported during the 30-day period following the vaccination at Month 6[4]

End point description:

An unsolicited AE is 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. An AE could, therefore, be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also included failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse. 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 = AE assessed by the investigator as causally related to the study vaccination.

End point type	Primary

End point timeframe:

During the 30-day period (i.e. from the day of vaccination up to 29 subsequent days) following the vaccination 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 AE(s)	18	13		
Grade 3 AE(s)	0	0		
Related AE(s)	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters at Day 42 by baseline ranges

End point title	Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters at Day 42 by baseline ranges[5]

End point description:

The parameters assessed were both biochemical (alanine aminotransferase = ALAT, creatinine = CREA, blood urea nitrogen = BUN) and haematological (basophils = BAS, eosinophils = EOS, red blood cells = RBC, hematocrit = HCT, hemoglobin = HGB, leukocytes [white blood cells] = WBC, lymphocytes = LYM, monocytes = MONO, neutrophils = NEU and platelets = PLA). Abnormal laboratory values at Day 42 were Below, Within and Above normal ranges, as compared to the baseline status of the same parameter, at Day 0 (Unknown, Below, Within and Above normal ranges) [e.g. ALAT Below (baseline) - Within (Day 42) = ALAT with below normal value at baseline and within normal values at Day 42].

End point type	Primary

End point timeframe:

At Day 42 (i.e. 42 days after the vaccination at Day 0)

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	74	73		
Units: Subjects				
ALAT, Unknown (baseline) - Below (Day 42) (N=2;2)	0	0		
ALAT, Unknown (baseline) - Within (Day 42) (N=2;2)	2	1		
ALAT, Unknown (baseline) - Above (Day 42) (N=2;2)	0	1		

ALAT, Below (baseline) - Below (Day 42) (N=2;1)	1	0		
ALAT, Below (baseline) - Within (Day 42) (N=2;1)	1	1		
ALAT, Below (baseline) - Above (Day 42) (N=2;1)	0	0		
ALAT, Within (baseline) - Below (Day 42) (N=66;62)	0	0		
ALAT, Within (baseline) -Within (Day 42) (N=66;62)	64	60		
ALAT, Within (baseline) - Above (Day 42) (N=66;62)	2	2		
ALAT, Above (baseline) - Below (Day 42) (N=4;7)	0	0		
ALAT, Above (baseline) - Within (Day 42) (N=4;7)	1	4		
ALAT, Above (baseline) - Above (Day 42) (N=4;7)	3	3		
BAS, Unknown (baseline) - Below (Day 42) (N=1;0)	0	0		
BAS, Unknown (baseline) - Within (Day 42) (N=1;0)	1	0		
BAS, Unknown (baseline) - Above (Day 42) (N=1;0)	0	0		
BAS, Below (baseline) - Below (Day 42) (N=0;0)	0	0		
BAS, Below (baseline) - Within (Day 42) (N=0;0)	0	0		
BAS, Below (baseline) - Above (Day 42) (N=0;0)	0	0		
BAS, Within (baseline) - Below (Day 42) (N=71;69)	0	0		
BAS, Within (baseline) - Within (Day 42) (N=71;69)	71	69		
BAS, Within (baseline) - Above (Day 42) (N=71;69)	0	0		
BAS, Above (baseline) - Below (Day 42) (N=0;4)	0	0		
BAS, Above (baseline) - Within (Day 42) (N=0;4)	0	4		
BAS, Above (baseline) - Above (Day 42) (N=0;4)	0	0		
CREA, Unknown (baseline) - Below (Day 42) (N=2;1)	0	1		
CREA, Unknown (baseline) - Within (Day 42) (N=2;1)	2	0		
CREA, Unknown (baseline) - Above (Day 42) (N=2;1)	0	0		
CREA, Below (baseline) - Below (Day 42) (N=30;27)	22	17		
CREA, Below (baseline) - Within (Day 42) (N=30;27)	8	10		
CREA, Below (baseline) - Above (Day 42) (N=30;27)	0	0		
CREA, Within (baseline) - Below (Day 42) (N=42;45)	7	12		
CREA, Within (baseline) -Within (Day 42) (N=42;45)	35	33		
CREA, Within (baseline) - Above (Day 42) (N=42;45)	0	0		
CREA, Above (baseline) - Below (Day 42) (N=0;0)	0	0		

CREA, Above (baseline) - Within (Day 42) (N=0;0)	0	0		
CREA, Above (baseline) - Above (Day 42) (N=0;0)	0	0		
EOS, Unknown (baseline) - Below (Day 42) (N=1;0)	0	0		
EOS, Unknown (baseline) - Within (Day 42) (N=1;0)	1	0		
EOS, Unknown (baseline) - Above (Day 42) (N=1;0)	0	0		
EOS, Below (baseline) - Below (Day 42) (N=1;0)	0	0		
EOS, Below (baseline) - Within (Day 42) (N=1;0)	1	0		
EOS, Below (baseline) - Above (Day 42) (N=1;0)	0	0		
EOS, Within (baseline) - Below (Day 42) (N=49;50)	1	1		
EOS, Within (baseline) - Within (Day 42) (N=49;50)	42	38		
EOS, Within (baseline) - Above (Day 42) (N=49;50)	6	11		
EOS, Above (baseline) - Below (Day 42) (N=21;23)	0	1		
EOS, Above (baseline) - Within (Day 42) (N=21;23)	4	10		
EOS, Above (baseline) - Above (Day 42) (N=21;23)	17	12		
RBC, Unknown (baseline) - Below (Day 42) (N=1;0)	0	0		
RBC, Unknown (baseline) - Within (Day 42) (N=1;0)	1	0		
RBC, Unknown (baseline) - Above (Day 42) (N=1;0)	0	0		
RBC, Below (baseline) - Below (Day 42) (N=5;5)	0	1		
RBC, Below (baseline) - Within (Day 42) (N=5;5)	5	4		
RBC, Below (baseline) - Above (Day 42) (N=5;5)	0	0		
RBC, Within (baseline) - Below (Day 42) (N=66;66)	5	2		
RBC, Within (baseline) - Within (Day 42) (N=66;66)	60	63		
RBC, Within (baseline) - Above (Day 42) (N=66;66)	1	1		
RBC, Above (baseline) - Below (Day 42) (N=0;2)	0	0		
RBC, Above (baseline) - Within (Day 42) (N=0;2)	0	1		
RBC, Above (baseline) - Above (Day 42) (N=0;2)	0	1		
HCT, Unknown (baseline) - Below (Day 42) (N=1;0)	0	0		
HCT, Unknown (baseline) - Within (Day 42) (N=1;0)	1	0		
HCT, Unknown (baseline) - Above (Day 42) (N=1;0)	0	0		
HCT, Below (baseline) - Below (Day 42) (N=25;24)	12	15		
HCT, Below (baseline) - Within (Day 42) (N=25;24)	13	8		

HCT, Below (baseline) - Above (Day 42) (N=25;24)	0	1		
HCT, Within (baseline) - Below (Day 42) (N=43;45)	5	2		
HCT, Within (baseline) - Within (Day 42) (N=43;45)	37	38		
HCT, Within (baseline) - Above (Day 42) (N=43;45)	1	5		
HCT, Above (baseline) - Below (Day 42) (N=3;4)	0	0		
HCT, Above (baseline) - Within (Day 42) (N=3;4)	2	4		
HCT, Above (baseline) - Above (Day 42) (N=3;4)	1	0		
HGB, Unknown (baseline) - Below (Day 42) (N=1;0)	0	0		
HGB, Unknown (baseline) - Within (Day 42) (N=1;0)	0	0		
HGB, Unknown (baseline) - Above (Day 42) (N=1;0)	1	0		
HGB, Below (baseline) - Below (Day 42) (N=20;14)	10	5		
HGB, Below (baseline) - Within (Day 42) (N=20;14)	10	9		
HGB, Below (baseline) - Above (Day 42) (N=20;14)	0	0		
HGB, Within (baseline) - Below (Day 42) (N=46;53)	4	7		
HGB, Within (baseline) - Within (Day 42) (N=46;53)	38	42		
HGB, Within (baseline) - Above (Day 42) (N=46;53)	4	4		
HGB, Above (baseline) - Below (Day 42) (N=5;6)	0	0		
HGB, Above (baseline) - Within (Day 42) (N=5;6)	3	5		
HGB, Above (baseline) - Above (Day 42) (N=5;6)	2	1		
WBC, Unknown (baseline) - Below (Day 42) (N=1;0)	0	0		
WBC, Unknown (baseline) - Within (Day 42) (N=1;0)	1	0		
WBC, Unknown (baseline) - Above (Day 42) (N=1;0)	0	0		
WBC, Below (baseline) - Below (Day 42) (N=5;7)	1	5		
WBC, Below (baseline) - Within (Day 42) (N=5;7)	3	1		
WBC, Below (baseline) - Above (Day 42) (N=5;7)	1	1		
WBC, Within (baseline) - Below (Day 42) (N=62;59)	2	1		
WBC, Within (baseline) - Within (Day 42) (N=62;59)	57	54		
WBC, Within (baseline) - Above (Day 42) (N=62;59)	3	4		
WBC, Above (baseline) - Below (Day 42) (N=4;7)	0	0		
WBC, Above (baseline) - Within (Day 42) (N=4;7)	1	4		
WBC, Above (baseline) - Above (Day 42) (N=4;7)	3	3		

LYM, Unknown (baseline) - Below (Day 42) (N=1;0)	0	0		
LYM, Unknown (baseline) - Within (Day 42) (N=1;0)	1	0		
LYM, Unknown (baseline) - Above (Day 42) (N=1;0)	0	0		
LYM, Below (baseline) - Below (Day 42) (N=7;10)	4	6		
LYM, Below (baseline) - Within (Day 42) (N=7;10)	2	2		
LYM, Below (baseline) - Above (Day 42) (N=7;10)	1	2		
LYM, Within (baseline) - Below (Day 42) (N=48;42)	7	2		
LYM, Within (baseline) - Within (Day 42) (N=48;42)	38	34		
LYM, Within (baseline) - Above (Day 42) (N=48;42)	3	6		
LYM, Above (baseline) - Below (Day 42) (N=16:21)	0	2		
LYM, Above (baseline) - Within (Day 42) (N=16:21)	5	5		
LYM, Above (baseline) - Above (Day 42) (N=16:21)	11	14		
MONO, Unknown (baseline) - Below (Day 42) (N=1;0)	1	0		
MONO, Unknown (baseline) - Within (Day 42) (N=1;0)	0	0		
MONO, Unknown (baseline) - Above (Day 42) (N=1;0)	0	0		
MONO, Below (baseline) - Below (Day 42) (N=8;9)	4	5		
MONO, Below (baseline) - Within (Day 42) (N=8;9)	4	4		
MONO, Below (baseline) - Above (Day 42) (N=8;9)	0	0		
MONO, Within (baseline) - Below (Day 42) (N=51;55)	3	2		
MONO, Within (baseline) -Within (Day 42) (N=51;55)	42	48		
MONO, Within (baseline) - Above (Day 42) (N=51;55)	6	5		
MONO, Above (baseline) - Below (Day 42) (N=12;9)	0	0		
MONO, Above (baseline) - Within (Day 42) (N=12;9)	6	3		
MONO, Above (baseline) - Above (Day 42) (N=12;9)	6	6		
NEU, Unknown (baseline) - Below (Day 42) (N=1;0)	0	0		
NEU, Unknown (baseline) - Within (Day 42) (N=1;0)	1	0		
NEU, Unknown (baseline) - Above (Day 42) (N=1;0)	0	0		
NEU, Below (baseline) - Below (Day 42) (N=15;21)	9	14		
NEU, Below (baseline) - Within (Day 42) (N=15;21)	6	6		
NEU, Below (baseline) - Above (Day 42) (N=15;21)	0	1		
NEU, Within (baseline) - Below (Day 42) (N=52;46)	4	6		

NEU, Within (baseline) - Within (Day 42) (N=52;46)	41	39		
NEU, Within (baseline) - Above (Day 42) (N=52;46)	7	1		
NEU, Above (baseline) - Within (Day 42) (N=4;6)	3	3		
NEU, Above (baseline) - Above (Day 42) (N=4;6)	1	3		
PLA, Unknown (baseline) - Below (Day 42) (N=2;0)	0	0		
PLA, Unknown (baseline) - Within (Day 42) (N=2;0)	2	0		
PLA, Unknown (baseline) - Above (Day 42) (N=2;0)	0	0		
PLA, Below (baseline) - Below (Day 42) (N=0;2)	0	0		
PLA, Below (baseline) - Within (Day 42) (N=0;2)	0	2		
PLA, Below (baseline) - Above (Day 42) (N=0;2)	0	0		
PLA, Within (baseline) - Below (Day 42) (N=59;56)	0	0		
PLA, Within (baseline) - Within (Day 42) (N=59;56)	51	52		
PLA, Within (baseline) - Above (Day 42) (N=59;56)	8	4		
PLA, Above (baseline) - Below (Day 42) (N=11;15)	0	0		
PLA, Above (baseline) - Within (Day 42) (N=11;15)	4	9		
PLA, Above (baseline) - Above (Day 42) (N=11;15)	7	6		
BUN, Unknown (baseline) - Below (Day 42) (N=2;1)	0	0		
BUN, Unknown (baseline) - Within (Day 42) (N=2;1)	2	1		
BUN, Unknown (baseline) - Above (Day 42) (N=2;1)	0	0		
BUN, Below (baseline) - Below (Day 42) (N=12;4)	4	1		
BUN, Below (baseline) - Within (Day 42) (N=12;4)	8	3		
BUN, Below (baseline) - Above (Day 42) (N=12;4)	0	0		
BUN, Within (baseline) - Below (Day 42) (N=54;62)	2	5		
BUN, Within (baseline) - Within (Day 42) (N=54;62)	50	57		
BUN, Within (baseline) - Above (Day 42) (N=54;62)	2	0		
BUN, Above (baseline) - Below (Day 42) (N=6;6)	0	0		
BUN, Above (baseline) - Within (Day 42) (N=6;6)	6	6		
BUN, Above (baseline) - Above (Day 42) (N=6;6)	0	0		
NEU, Above (baseline) - Below (Day 42) (N=4;6)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters at Month 7 by baseline ranges

End point title	Number of subjects with clinically relevant abnormalities in biochemical and haematological parameters at Month 7 by baseline ranges[6]

End point description:

The parameters assessed were both biochemical (alanine aminotransferase = ALAT, creatinine = CREA, blood urea nitrogen = BUN) and haematological (basophils = BAS, eosinophils = EOS, red blood cells = RBC, hematocrit = HCT, hemoglobin = HGB, leukocytes [white blood cells] = WBC, lymphocytes = LYM, monocytes = MONO, neutrophils = NEU and platelets = PLA). Abnormal laboratory values at Month 7 were Below, Within and Above normal ranges, as compared to the baseline status of the same parameter, at Day 0 (Unknown, Below, Within and Above normal ranges) [e.g. ALAT Below (baseline) - Within (Month 7) = ALAT with below normal value at baseline and within normal values at Month 7].

End point type	Primary

End point timeframe:

At Month 7 (i.e. 30 days after the vaccination at Month 6)

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	74	72		
Units: Subjects				
ALAT, Unknown (baseline) -Below (Month 7) (N=2;2)	0	0		
ALAT, Unknown (baseline) -Within (Month 7) (N=2;2)	2	2		
ALAT, Unknown (baseline) -Above (Month 7) (N=2;2)	0	0		
ALAT, Below (baseline) - Below (Month 7) (N=2;1)	1	0		
ALAT, Below (baseline) -Within (Month 7) (N=2;1)	1	1		
ALAT, Below (baseline) -Above (Month 7) (N=2;1)	0	0		
ALAT, Within(baseline) -Below (Month 7) (N=65;62)	1	1		
ALAT, Within(baseline) -Within (Month 7) (N=65;62)	64	60		
ALAT, Within (baseline) -Above (Month 7) (N=65;62)	0	1		
ALAT, Above (baseline) - Below (Month 7) (N=4;7)	0	0		
ALAT, Above (baseline) -Within (Month 7) (N=4;7)	3	7		
ALAT, Above (baseline) - Above (Month 7) (N=4;7)	1	0		
BAS, Unknown (baseline) -Below (Month 7) (N=1;0)	0	0		
BAS, Unknown (baseline) -Within (Month 7) (N=1;0)	1	0		
BAS, Unknown (baseline) - Above (Month 7) (N=1;0)	0	0		

BAS, Below (baseline) - Below (Month 7) (N=0;0)	0	0		
BAS, Below (baseline) - Within (Month 7) (N=0;0)	0	0		
BAS, Below (baseline) - Above (Month 7) (N=0;0)	0	0		
BAS, Within (baseline) -Below (Month 7) (N=73;68)	0	0		
BAS, Within (baseline) -Within (Month 7) (N=73;68)	72	67		
BAS, Within (baseline) - Above (Month 7) (N=73;68)	1	1		
BAS, Above (baseline) - Below (Month 7) (N=0;4)	0	0		
BAS, Above (baseline) -Within (Month 7) (N=0;4)	0	2		
BAS, Above (baseline) - Above (Month 7) (N=0;4)	0	2		
CREA, Unknown(baseline) -Below (Month 7) (N=2;1)	1	1		
CREA, Unknown(baseline) -Within (Month 7) (N=2;1)	1	0		
CREA, Unknown(baseline) -Above (Month 7) (N=2;1)	0	0		
CREA, Below(baseline) -Below (Month 7) (N=29;26)	23	21		
CREA, Below(baseline) -Within (Month 7) (N=29;26)	6	5		
CREA, Below(baseline) -Above (Month 7) (N=29;26)	0	0		
CREA, Within(baseline) -Below (Month 7) (N=42;45)	8	9		
CREA, Within(baseline) -Within (Month 7) (N=42;45)	34	36		
CREA, Within(baseline) -Above (Month 7) (N=42;45)	0	0		
CREA, Above(baseline) -Below (Month 7) (N=0;0)	0	0		
CREA, Above(baseline) -Within (Month 7) (N=0;0)	0	0		
CREA, Above(baseline) -Above (Month 7) (N=0;0)	0	0		
EOS, Unknown (baseline) -Below (Month 7) (N=1;0)	0	0		
EOS, Unknown (baseline) -Within (Month 7) (N=1;0)	1	0		
EOS, Unknown (baseline) -Above (Month 7) (N=1;0)	0	0		
EOS, Below (baseline) - Below (Month 7) (N=1;0)	0	0		
EOS, Below (baseline) -Within (Month 7) (N=1;0)	1	0		
EOS, Below (baseline) - Above (Month 7) (N=1;0)	0	0		
EOS, Within (baseline) -Below (Month 7) (N=51;49)	0	1		
EOS, Within (baseline) -Within (Month 7) (N=51;49)	42	38		
EOS, Within (baseline) -Above (Month 7) (N=51;49)	9	10		
EOS, Above (baseline) - Below (Month 7) (N=21;23)	0	0		

EOS, Above (baseline) -Within (Month 7) (N=21;23)	3	10		
EOS, Above (baseline) - Above (Month 7) (N=21;23)	18	13		
RBC, Unknown (baseline) -Below (Month 7) (N=1;0)	0	0		
RBC, Unknown (baseline) -Within (Month 7) (N=1;0)	1	0		
RBC, Unknown (baseline) -Above (Month 7) (N=1;0)	0	0		
RBC, Below (baseline) - Below (Month 7) (N=5;5)	1	2		
RBC, Below (baseline) -Within (Month 7) (N=5;5)	4	3		
RBC, Below (baseline) - Above (Month 7) (N=5;5)	0	0		
RBC, Within (baseline) -Below (Month 7) (N=68;65)	4	4		
RBC, Within (baseline) -Within (Month 7) (N=68;65)	63	61		
RBC, Within (baseline) -Above (Month 7) (N=68;65)	1	0		
RBC, Above (baseline) - Below (Month 7) (N=0;2)	0	0		
RBC, Above (baseline) -Within (Month 7) (N=0;2)	0	1		
RBC, Above (baseline) - Above (Month 7) (N=0;2)	0	1		
HCT, Unknown (baseline) - Below (Month 7) (N=1;0)	0	0		
HCT, Unknown (baseline) -Within (Month 7) (N=1;0)	0	0		
HCT, Unknown (baseline) -Above (Month 7) (N=1;0)	1	0		
HCT, Below (baseline) - Below (Month 7) (N=26;24)	15	15		
HCT, Below (baseline) -Within (Month 7) (N=26;24)	11	9		
HCT, Below (baseline) - Above (Month 7) (N=25;24)	0	0		
HCT, Within (baseline) -Below (Month 7) (N=44;44)	2	4		
HCT, Within (baseline) -Within (Month 7) (N=44;44)	41	40		
HCT, Within (baseline) - Above (Month 7) (N=44;44)	1	0		
HCT, Above (baseline) - Below (Month 7) (N=3;4)	0	0		
HCT, Above (baseline) -Within (Month 7) (N=3;4)	3	4		
HCT, Above (baseline) - Above (Month 7) (N=3;4)	0	0		
HGB, Unknown (baseline) -Below (Month 7) (N=1;0)	0	0		
HGB, Unknown (baseline) -Within (Month 7) (N=1;0)	0	0		
HGB, Unknown (baseline) -Above (Month 7) (N=1;0)	1	0		
HGB, Below (baseline) - Below (Month 7) (N=21;14)	10	7		
HGB, Below (baseline) -Within (Month 7) (N=21;14)	11	7		

HGB, Below (baseline) - Above (Month 7) (N=21;14)	0	0		
HGB, Within (baseline) - Below (Month 7) (N=47;52)	1	7		
HGB, Within (baseline) -Within (Month 7) (N=47;52)	40	44		
HGB, Within (baseline) - Above (Month 7) (N=47;52)	6	1		
HGB, Above (baseline) - Below (Month 7) (N=5;6)	0	0		
HGB, Above (baseline) -Within (Month 7) (N=5;6)	3	5		
HGB, Above (baseline) - Above (Month 7) (N=5;6)	2	1		
WBC, Unknown (baseline) -Below (Month 7) (N=1;0)	0	0		
WBC, Unknown (baseline) -Within (Month 7) (N=1;0)	1	0		
WBC, Unknown (baseline) -Above (Month 7) (N=1;0)	0	0		
WBC, Below (baseline) - Below (Month 7) (N=5;7)	3	4		
WBC, Below (baseline) -Within (Month 7) (N=5;7)	2	3		
WBC, Below (baseline) - Above (Month 7) (N=5;7)	0	0		
WBC, Within (baseline) - Below (Month 7) (N=63;58)	1	7		
WBC, Within (baseline) -Within (Month 7) (N=63;58)	59	48		
WBC, Within (baseline) - Above (Month 7) (N=63;58)	3	3		
WBC, Above (baseline) - Below (Month 7) (N=5;7)	0	0		
WBC, Above (baseline) -Within (Month 7) (N=5;7)	3	5		
WBC, Above (baseline) - Above (Month 7) (N=5;7)	2	2		
LYM, Unknown (baseline) -Below (Month 7) (N=1;0)	0	0		
LYM, Unknown (baseline) -Within (Month 7) (N=1;0)	1	0		
LYM, Unknown (baseline) -Above (Month 7) (N=1;0)	0	0		
LYM, Below (baseline) - Below (Month 7) (N=7;10)	5	6		
LYM, Below (baseline) -Within (Month 7) (N=7;10)	1	3		
LYM, Below (baseline) - Above (Month 7) (N=7;10)	1	1		
LYM, Within (baseline) - Below (Month 7) (N=49;42)	6	5		
LYM, Within (baseline) -Within (Month 7) (N=49;42)	37	36		
LYM, Within (baseline) - Above (Month 7) (N=49;42)	6	1		
LYM, Above (baseline) - Below (Month 7) (N=17;20)	1	1		
LYM, Above (baseline) -Within (Month 7) (N=17;20)	10	8		
LYM, Above (baseline) - Above (Month 7) (N=17;20)	6	11		

MONO, Unknown (baseline) -Below (Month 7) (N=1;0)	1	0		
MONO, Unknown(baseline) -Within (Month 7) (N=1;0)	0	0		
MONO, Unknown(baseline) -Above (Month 7) (N=1;0)	0	0		
MONO, Below (baseline) - Below (Month 7) (N=8;9)	2	4		
MONO, Below(baseline) -Within (Month 7) (N=8;9)	6	4		
MONO, Below (baseline) - Above (Month 7) (N=8;9)	0	1		
MONO, Within(baseline) -Below (Month 7) (N=53;54)	4	3		
MONO, Within(baseline) -Within (Month 7) (N=53;54)	49	51		
MONO, Within(baseline) -Above (Month 7) (N=53;54)	0	0		
MONO, Above(baseline) -Below (Month 7) (N=12;9)	0	0		
MONO, Above(baseline) -Within (Month 7) (N=12;9)	11	7		
MONO, Above(baseline) -Above (Month 7) (N=12;9)	1	2		
NEU, Unknown(baseline) -Below (Month 7) (N=1;0)	0	0		
NEU, Unknown(baseline) -Within (Month 7) (N=1;0)	1	0		
NEU, Unknown(baseline) -Above (Month 7) (N=1;0)	0	0		
NEU, Below (baseline) - Below (Month 7) (N=16;21)	5	10		
NEU, Below(baseline) -Within (Month 7) (N=16;21)	10	10		
NEU, Below (baseline) - Above (Month 7) (N=16;21)	1	1		
NEU, Within(baseline) -Below (Month 7) (N=53;45)	4	4		
NEU, Within(baseline) -Within (Month 7) (N=53;45)	43	35		
NEU, Within(baseline) -Above (Month 7) (N=53;45)	6	6		
NEU, Above(baseline) -Below (Month 7) (N=4;6)	0	1		
NEU, Above(baseline) -Within (Month 7) (N=4;6)	2	2		
NEU, Above(baseline) -Above (Month 7) (N=4;6)	2	3		
PLA, Unknown(baseline) -Below (Month 7) (N=2;0)	0	0		
PLA, Unknown(baseline) -Within (Month 7) (N=2;0)	2	0		
PLA, Unknown(baseline) -Above (Month 7) (N=2;0)	0	0		
PLA, Below (baseline) -Below (Month 7) (N=0;2)	0	0		
PLA, Below (baseline) -Within (Month 7) (N=0;2)	0	2		
PLA, Below (baseline) -Above (Month 7) (N=0;2)	0	0		
PLA, Within (baseline) -Below (Month 7) (N=60;55)	0	0		

PLA, Within (baseline) -Within (Month 7) (N=60;55)	56	53		
PLA, Within (baseline) -Above (Month 7) (N=60;55)	4	2		
PLA, Above (baseline) - Below (Month 7) (N=12;15)	0	0		
PLA, Above (baseline) -Within (Month 7) (N=12;15)	7	8		
PLA, Above (baseline) - Above (Month 7) (N=12;15)	5	7		
BUN, Unknown (baseline) -Below (Month 7) (N=2;1)	0	0		
BUN, Unknown (baseline) -Within (Month 7) (N=2;1)	2	1		
BUN, Unknown (baseline) -Above (Month 7) (N=2;1)	0	0		
BUN, Below (baseline) - Below (Month 7) (N=12;4)	5	0		
BUN, Below (baseline) -Within (Month 7) (N=12;4)	7	4		
BUN, Below (baseline) - Above (Month 7) (N=12;4)	0	0		
BUN, Within (baseline) -Below (Month 7) (N=52;61)	4	10		
BUN, Within(baseline) -Within (Month 7) (N=52;61)	47	51		
BUN, Within (baseline) -Above (Month 7) (N=52;61)	1	0		
BUN, Above (baseline) - Below (Month 7) (N=6;6)	0	0		
BUN, Above (baseline) -Within (Month 7) (N=6;6)	6	6		
BUN, Above (baseline) - Above (Month 7) (N=6;6)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with serious adverse events (SAEs) from Day 0 up to Month 7

End point title	Number of subjects with serious adverse events (SAEs) from Day 0 up to Month 7[7]

End point description:

SAEs assessed included medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of existing hospitalization resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Primary

End point timeframe:

From Day 0 up to Month 7 (i.e. from first vaccination at Day 0 up to 30 days after the second vaccination at Month 6)

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				
SAE(s)	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with AEs and SAEs leading to withdrawal from Day 0 up to Month 7

End point title	Number of subjects with AEs and SAEs leading to withdrawal from Day 0 up to Month 7[8]

End point description:

The number of subjects with AEs and SAEs leading to premature discontinuation of the study was assessed.

End point type	Primary

End point timeframe:

From Day 0 up to Month 7 (i.e. from first vaccination at Day 0 up to 30 days after the second vaccination at Month 6)

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				
AE(s) and SAE(s) leading to withdrawal	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with potential immune-mediated diseases (pIMDs) from Day 0 up to Month 7

End point title	Number of subjects with potential immune-mediated diseases (pIMDs) from Day 0 up to Month 7[9]

End point description:

pIMDs were defined as a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which might or might not have an autoimmune aetiology.

End point type	Primary

End point timeframe:

From Day 0 up to Month 7 (i.e. from first vaccination at Day 0 up to 30 days after the second vaccination at Month 6)

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				
pIMD(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with medically significant conditions (MSCs) from Day 0 up to Month 7

End point title	Number of subjects with medically significant conditions (MSCs) from Day 0 up to Month 7[10]

End point description:

MSCs were defined as AEs prompting emergency room or physician visits that were not related to common diseases or were not routine visits for physical examination or vaccination and as SAEs that were not related to common diseases. Common diseases included: upper respiratory tract infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, and injury.

End point type	Primary

End point timeframe:

From Day 0 up to Month 7 (i.e. from first vaccination at Day 0 up to 30 days after the second vaccination at Month 6)

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				
MSC(s)	37	28		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted subjects for HPV-16 and HPV-18 antigens at Month 7

End point title	Number of seroconverted subjects for HPV-16 and HPV-18 antigens at Month 7[11]

End point description:

Seroconversion was defined as a titer greater than or equal to the cut-off value in the serum of seronegative subjects, defined as subjects who had an antibody titer below the cut-off value before vaccination. Titers were measured by Enzyme Linked Immunosorbent Assay (ELISA) and the cut-offs were 19 ELISA Units per milliliter (EU/mL) for HPV-16 and 18 EU/mL for HPV-18.

End point type	Primary

End point timeframe:

At Month 7 (i.e. 30 days after the vaccination at Month 6)

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	64	44		
Units: Subjects				
Anti-HPV-16 (N=64;43)	64	1		
Anti-HPV-18 (N=62;44)	62	1		

Statistical analyses

No statistical analyses for this end point

Primary: Anti-HPV-16/18 antibody concentrations at Month 7

End point title	Anti-HPV-16/18 antibody concentrations at Month 7[12]

End point description:

Antibody concentrations were assessed by ELISA and expressed as geometric mean concentrations (GMCs) in EU/mL.

End point type	Primary

End point timeframe:

At Month 7 (i.e. 30 days after the vaccination at Month 6)

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	64	44		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16 (N=64;43)	20080.0 (16831.8 to 23954.9)	10.4 (8.7 to 12.5)		
Anti-HPV-18 (N=62;44)	10621.8 (8865.3 to 12726.3)	9.6 (8.4 to 11.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for HPV-16 and HPV-18 antigens at Month 7, Month 12 (for both groups) and at Month 18, Month 24 and Month 36 (only for Cervarix Group)

End point title	Number of seroconverted subjects for HPV-16 and HPV-18 antigens at Month 7, Month 12 (for both groups) and at Month 18, Month 24 and Month 36 (only for Cervarix Group)

End point description:

Seroconversion was defined as a titer greater than or equal to the cut-off value in the serum of seronegative subjects, defined as subjects who had an antibody titer below the cut-off value before vaccination. Titers were measured by ELISA and the cut-offs were 19 EU/mL for HPV-16 and 18 EU/mL for HPV-18. Note: Month 7 data are also reported in the Primary outcome measure.

End point type	Secondary

End point timeframe:

At Month 7, Month 12 (for both groups) and at Month 18, Month 24 and Month 36 (only for Cervarix Group)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	49		
Units: Subjects				
Anti-HPV-16, Month 7 (N=64;43)	64	1		
Anti-HPV-16, Month 12 (N=65;48)	65	1		
Anti-HPV-16, Month 18 (N=66;0)	66	0		
Anti-HPV-16, Month 24 (N=67;0)	67	0		
Anti-HPV-16, Month 36 (N=67;0)	67	0		
Anti-HPV-18, Month 7 (N=62;44)	62	1		
Anti-HPV-18, Month 12 (N=63;49)	63	0		
Anti-HPV-18, Month 18 (N=64;0)	64	0		
Anti-HPV-18, Month 24 (N=65;0)	65	0		
Anti-HPV-18, Month 36 (N=65;0)	65	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HPV-16 and anti-HPV-18 antibody concentrations at Month 7, Month 12 (for both groups) and at Month 18, Month 24 and Month 36 (only for Cervarix Group)

End point title	Anti-HPV-16 and anti-HPV-18 antibody concentrations at Month 7, Month 12 (for both groups) and at Month 18, Month 24 and Month 36 (only for Cervarix Group)

End point description:

Antibody concentrations were assessed by ELISA and expressed as GMCs in EU/mL. Note: Month 7 data are also reported in the Primary outcome measure.

End point type	Secondary

End point timeframe:

At Month 7, Month 12 (for both groups) and at Month 18, Month 24 and Month 36 (only for Cervarix Group)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	49		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-HPV-16, Month 7 (N=64;43)	20080.0 (16831.8 to 23954.9)	10.4 (8.7 to 12.5)		
Anti-HPV-16, Month 12 (N=65;48)	3246.5 (2617.4 to 4026.8)	9.7 (9.3 to 10.2)		
Anti-HPV-16, Month 18 (N=66;0)	2800.5 (2325.8 to 3372.0)	0 (0 to 0)		
Anti-HPV-16, Month 24 (N=67;0)	1951.9 (1553.7 to 2452.2)	0 (0 to 0)		
Anti-HPV-16, Month 36 (N=67;0)	1680.6 (1384.2 to 2040.4)	0 (0 to 0)		
Anti-HPV-18, Month 7 (N=62;44)	10621.8 (8865.3 to 12726.3)	9.6 (8.4 to 11.1)		
Anti-HPV-18, Month 12 (N=63;49)	1216.6 (953.1 to 1553.0)	9.0 (9.0 to 9.0)		
Anti-HPV-18, Month 18 (N=64;0)	802.9 (632.4 to 1019.5)	0 (0 to 0)		
Anti-HPV-18, Month 24 (N=64;0)	766.6 (603.3 to 974.2)	0 (0 to 0)		
Anti-HPV-18, Month 36 (N=65;0)	536.4 (420.6 to 684.0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for measles antigen

End point title	Number of seropositive subjects for measles antigen

End point description:

A seropositive subject was defined as a subject whose anti-measles antibody titer was equal to or above

(≥) 150 milli-International Units per milliliter (mIU/mL), as assessed by ELISA.

End point type	Secondary

End point timeframe:

At Day 0 and Day 42 (i.e. 42 days after the vaccination at Day 0)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	58		
Units: Subjects				
Anti-measles, Day 0 (N=66;55)	65	50		
Anti-measles, Day 42 (N=68;58)	67	58		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-measles antibody concentrations

End point title	Anti-measles antibody concentrations

End point description:

Anti-measles antibody concentrations were measured by ELISA, expressed as GMCs, in mIU/mL. The cut-off of the assay was an anti-measles antibody concentration ≥ 150 mIU/mL.

End point type	Secondary

End point timeframe:

At Day 0 and Day 42 (i.e. 42 days after the vaccination at Day 0)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	58		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-measles, Day 0 (N=66;55)	1029.8 (852.8 to 1243.6)	694.8 (524.0 to 921.3)		
Anti-measles, Day 42 (N=68;58)	897.1 (748.8 to 1074.8)	2512.3 (2140.3 to 2949.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for mumps antigen

End point title	Number of seropositive subjects for mumps antigen

End point description:

A seropositive subject was defined as a subject whose anti-mumps antibody titer was ≥ 231 U/mL, as assessed by ELISA.

End point type	Secondary

End point timeframe:

At Day 0 and Day 42 (i.e. 42 days after the vaccination at Day 0)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	58		
Units: Subjects				
Anti-mumps, Day 0 (N=66;55)	64	50		
Anti-mumps, Day 42 (N=68;58)	66	57		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-mumps antibody concentrations

End point title	Anti-mumps antibody concentrations

End point description:

Anti-mumps antibody concentrations were measured by ELISA, expressed as GMCs, in U/mL. The cut-off of the assay was an anti-mumps antibody concentration ≥ 231 U/mL.

End point type	Secondary

End point timeframe:

At Day 0 and Day 42 (i.e. 42 days after the vaccination at Day 0)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	58		
Units: U/mL				
geometric mean (confidence interval 95%)				
Anti-mumps, Day 0 (N=66;55)	3613.7 (2742.1 to 4762.4)	2142.6 (1492.7 to 3075.5)		
Anti-mumps, Day 42 (N=68;58)	3594.1 (2749.1 to 4698.8)	7001.1 (5414.9 to 9052.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for rubella antigen

End point title	Number of seropositive subjects for rubella antigen

End point description:

A seropositive subject was defined as a subject whose anti-rubella antibody titer was ≥ 4 IU/mL, as assessed by ELISA.

End point type	Secondary

End point timeframe:

At Day 0 and Day 42 (i.e. 42 days after the vaccination at Day 0)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	58		
Units: Subjects				
Anti-rubella, Day 0 (N=66;55)	66	53		
Anti-rubella, Day 42 (N=68;58)	68	58		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rubella antibody concentrations

End point title	Anti-rubella antibody concentrations

End point description:

Anti-rubella antibody concentrations were measured by ELISA, expressed as GMCs, in IU/mL. The cut-off of the assay was an anti-rubella antibody concentration ≥ 4 IU/mL.

End point type	Secondary

End point timeframe:

At Day 0 and Day 42 (i.e. 42 days after the vaccination at Day 0)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	58		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-rubella, Day 0 (N=66;55)	82.0 (69.4 to 96.8)	48.9 (36.3 to 65.9)		
Anti-rubella, Day 42 (N=68;58)	79.3 (67.3 to 93.6)	124.2 (107.0 to 144.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against diphtheria and tetanus antigens

End point title	Number of seroprotected subjects against diphtheria and tetanus antigens

End point description:

A seroprotected subject against diphtheria antigen was defined as a subject with an anti-diphtheria (anti-D) antibody concentration ≥ the cut-off of 0.1 IU/mL, as measured by ELISA. A seroprotected subject against tetanus antigen was defined as a subject with an anti-tetanus (anti-T) antibody concentration ≥ the cut-off of 0.1 IU/mL, as measured by ELISA.

End point type	Secondary

End point timeframe:

At Month 7 (i.e. 30 days after the vaccination at Month 6)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	47		
Units: Subjects				
Anti-D	45	47		
Anti-T	60	47		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with pIMDs from Day 0 up to Month 12

End point title	Number of subjects with pIMDs from Day 0 up to Month 12

End point description:

pIMDs are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which might or might not have an autoimmune aetiology.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 12 (i.e. from first vaccination at Day 0 up to 6 months after the second 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				
pIMD(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with MSCs from Day 0 up to Month 12

End point title	Number of subjects with MSCs from Day 0 up to Month 12

End point description:

MSCs were defined as AEs prompting emergency room or physician visits that were not related to common diseases or were not routine visits for physical examination or vaccination and as SAEs that were not related to common diseases. Common diseases included: upper respiratory tract infections, sinusitis, pharyngitis, gastroenteritis, urinary tract infections, and injury.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 12 (i.e. from first vaccination at Day 0 up to 6 months after the second 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				
MSC(s)	38	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with SAEs from Day 0 up to Month 12

End point title	Number of subjects with SAEs from Day 0 up to Month 12

End point description:

SAEs assessed include medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 12 (i.e. from first vaccination at Day 0 up to 6 months after the second 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				
SAE(s)	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with SAEs related to the investigational products or any fatal SAE

End point title	Number of subjects with SAEs related to the investigational products or any fatal SAE

End point description:

SAEs assessed included medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

Throughout the study period (i.e. from Day 0 up to Month 12 for Priorix + Infanrix Group and from Day 0 up to Month 36 for Cervarix Group)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects				
Related SAE(s)	0	0		
Fatal SAE(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with AEs/SAEs leading to withdrawal throughout the study period

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

	throughout the study period

End point description:

The number of subjects with AEs and SAEs leading to premature discontinuation of the study was assessed.

End point type	Secondary

End point timeframe:

Throughout the study period (i.e from Day 0 up to Month 12 for Priorix + Infanrix Group and from Day 0 up to Month 36 for Cervarix Group)

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	74		
Units: Subjects				
AE(s)/SAE(s) leading to withdrawal	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting the intake of concomitant medication during the 43-day period following the vaccination at Day 0

End point title	Number of subjects reporting the intake of concomitant medication during the 43-day period following the vaccination at Day 0

End point description:

Concomitant medication taken at least once during the 43-day period (i.e. from the day of vaccination up to 42 subsequent days) following the vaccination at Day 0 included: any type of medicines, antipyretics, prophylactic antipyretics, and antibiotics.

End point type	Secondary

End point timeframe:

During the 43-day period (i.e. from the day of vaccination up to 42 subsequent days) following the vaccination at 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				
Any medication	45	36		
Any antipyretic	29	24		
Prophylactic antipyretic	0	0		
Any antibiotic	18	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting the intake of concomitant medication during the 30-day period following the vaccination at Month 6

End point title	Number of subjects reporting the intake of concomitant medication during the 30-day period following the vaccination at Month 6

End point description:

Concomitant medication taken at least once during the 30-day period (i.e. from the day of vaccination up to 29 subsequent days) following the vaccination at Month 6 included: any type of medicines, antipyretics, prophylactic antipyretics, and antibiotics.

End point type	Secondary

End point timeframe:

During the 30-day period (i.e. from the day of vaccination up to 29 subsequent days) following the vaccination at Month 6

End point values	Cervarix Group	Priorix + Infanrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	71		
Units: Subjects				
Any medication	19	23		
Any antipyretic	10	8		
Prophylactic antipyretic	0	0		
Any antibiotic	6	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects completing the vaccination schedule in both groups

End point title	Percentage of subjects completing the vaccination schedule in both groups

End point description:

The percentage of subjects who received the specified total number of doses (dose 1, dose 2, any dose) is reported.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 6 (i.e. from first vaccination at Day 0 up to the second 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: Percentage of subjects				
number (not applicable)				
Subjects receiving only 1 dose	0	4.1		
Subjects receiving 2 doses	100	95.9		
Subjects receiving at least 1 dose	100	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related to vaccination solicited fever, measles/rubella-like rash, parotid gland swelling and signs of meningism including febrile convulsion

End point title	Number of subjects with any, grade 3 and related to vaccination solicited fever, measles/rubella-like rash, parotid gland swelling and signs of meningism including febrile convulsion

End point description:

Measles/Rubella-like rash: the presence of macules, discolored small patches or spots of the skin, neither elevated nor depressed below the skin's surface and/or papules, raised bumps on the skin usually below (<) 1 cm in diameter. Parotid/salivary gland swelling: swelling/tenderness in the mandibular/submandibular region. Suspected signs of meningism including febrile convulsions: febrile convulsions or any other neurological signs or symptoms indicative of meningism. Any = occurrence of any solicited symptom regardless of their intensity grade or relationship to vaccination. Any fever = axillary temperature equal to or above (≥) 37.5°C. Grade 3 AE = AE which prevented normal, everyday activities. Grade 3 measles/rubella-like rash = more than 150 lesions. Grade 3 parotid gland swelling = swelling with accompanying general symptoms. Grade 3 fever = axillary temperature above (>) 39.0°C. Related = any symptom assessed by the investigator as causally related to the vaccination.

End point type	Secondary

End point timeframe:

During the 43-day period (i.e. from the day of vaccination up to 42 subsequent days) following the vaccination at 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				
Any Fever	30	27		
Grade 3 Fever	7	2		
Related Fever	6	7		
Any Measles/Rubella-like rash	1	1		
Grade 3 Measles/Rubella-like rash	0	0		
Related Measles/Rubella-like rash	1	1		
Any Parotid gland swelling	0	0		
Grade 3 Parotid gland swelling	0	0		
Related 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 AEs: During the 7-day period after each vaccination. Unsolicited AEs: During the 43-day period after the vaccination at Day 0 and during the 30-day period after the vaccination at Month 6. SAEs: From Day 0 up to Month 12.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Cervarix Group

Reporting group description:

Healthy female subjects aged between, and including, 4 and 6 years, who received two doses of Cervarix vaccine at Day 0 and Month 6.

Reporting group title	Priorix + Infanrix Group

Reporting group description:

Healthy female subjects aged between, and including, 4 and 6 years, who received one dose of Priorix vaccine at Day 0 and one dose of Infanrix vaccine 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			
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: 0 %

Non-serious adverse events	Cervarix Group	Priorix + Infanrix Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 74 (94.59%)	65 / 74 (87.84%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	15 / 74 (20.27%)	10 / 74 (13.51%)	
occurrences (all)	17	14	
Influenza like illness			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	54 / 74 (72.97%)	40 / 74 (54.05%)	
occurrences (all)	88	51	
Pyrexia			
subjects affected / exposed	36 / 74 (48.65%)	33 / 74 (44.59%)	
occurrences (all)	39	39	
Swelling			
subjects affected / exposed	19 / 74 (25.68%)	18 / 74 (24.32%)	
occurrences (all)	22	21	
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	3 / 74 (4.05%)	0 / 74 (0.00%)	
occurrences (all)	3	0	
Asthma			
subjects affected / exposed	2 / 74 (2.70%)	3 / 74 (4.05%)	
occurrences (all)	2	3	
Asthmatic crisis			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Bronchial hyperreactivity			

subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	2 / 74 (2.70%)	1 / 74 (1.35%)	
occurrences (all)	3	1	
Epistaxis			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	1 / 74 (1.35%)	1 / 74 (1.35%)	
occurrences (all)	2	1	
Rhinorrhoea			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Vasomotor rhinitis			
subjects affected / exposed	1 / 74 (1.35%)	1 / 74 (1.35%)	
occurrences (all)	1	1	
Psychiatric disorders			
Irritability			
subjects affected / exposed	22 / 74 (29.73%)	19 / 74 (25.68%)	
occurrences (all)	31	24	
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Clavicle fracture			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Contusion			

subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Head injury			
subjects affected / exposed	1 / 74 (1.35%)	1 / 74 (1.35%)	
occurrences (all)	1	1	
Mouth injury			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Multiple injuries			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Stab wound			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	18 / 74 (24.32%)	25 / 74 (33.78%)	
occurrences (all)	25	35	
Meningism			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	16 / 74 (21.62%)	15 / 74 (20.27%)	
occurrences (all)	23	16	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Eye disorders			

Conjunctivitis allergic			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Eye allergy			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 74 (1.35%)	1 / 74 (1.35%)	
occurrences (all)	1	1	
Anal fissure			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	0 / 74 (0.00%)	2 / 74 (2.70%)	
occurrences (all)	0	2	
Dyspepsia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Food poisoning			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorder			
subjects affected / exposed	11 / 74 (14.86%)	16 / 74 (21.62%)	
occurrences (all)	11	21	
Nausea			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	3 / 74 (4.05%)	1 / 74 (1.35%)	
occurrences (all)	4	1	
Dermatitis atopic			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	18 / 74 (24.32%)	18 / 74 (24.32%)	
occurrences (all)	22	19	
Rash			
subjects affected / exposed	6 / 74 (8.11%)	5 / 74 (6.76%)	
occurrences (all)	6	5	
Rash morbilliform			
subjects affected / exposed	1 / 74 (1.35%)	1 / 74 (1.35%)	
occurrences (all)	1	1	
Skin lesion			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	10 / 74 (13.51%)	7 / 74 (9.46%)	
occurrences (all)	10	7	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 74 (17.57%)	11 / 74 (14.86%)	
occurrences (all)	15	16	
Myalgia			
subjects affected / exposed	21 / 74 (28.38%)	14 / 74 (18.92%)	
occurrences (all)	26	20	
Neck pain			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			

subjects affected / exposed	1 / 74 (1.35%)	1 / 74 (1.35%)	
occurrences (all)	1	1	
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	2 / 74 (2.70%)	0 / 74 (0.00%)	
occurrences (all)	2	0	
Bronchitis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	5 / 74 (6.76%)	7 / 74 (9.46%)	
occurrences (all)	5	7	
Giardiasis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Gingival abscess			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Hordeolum			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Impetigo			
subjects affected / exposed	3 / 74 (4.05%)	0 / 74 (0.00%)	
occurrences (all)	3	0	
Infection parasitic			
subjects affected / exposed	1 / 74 (1.35%)	2 / 74 (2.70%)	
occurrences (all)	1	2	
Influenza			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	

Lice infestation			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	24 / 74 (32.43%)	27 / 74 (36.49%)	
occurrences (all)	28	33	
Otitis externa			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Otitis media			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Otitis media acute			
subjects affected / exposed	2 / 74 (2.70%)	1 / 74 (1.35%)	
occurrences (all)	2	1	
Pharyngitis			
subjects affected / exposed	6 / 74 (8.11%)	4 / 74 (5.41%)	
occurrences (all)	6	4	
Pneumonia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Pyoderma			
subjects affected / exposed	0 / 74 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	1 / 74 (1.35%)	2 / 74 (2.70%)	
occurrences (all)	1	2	
Sinusitis			
subjects affected / exposed	4 / 74 (5.41%)	0 / 74 (0.00%)	
occurrences (all)	4	0	
Tinea pedis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Tooth abscess			
subjects affected / exposed	2 / 74 (2.70%)	1 / 74 (1.35%)	
occurrences (all)	2	1	

Urinary tract infection subjects affected / exposed occurrences (all)	0 / 74 (0.00%) 0	1 / 74 (1.35%) 1	
Viral infection subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 2	2 / 74 (2.70%) 3	
Vulvovaginitis subjects affected / exposed occurrences (all)	1 / 74 (1.35%) 1	1 / 74 (1.35%) 1	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	21 / 74 (28.38%) 24	13 / 74 (17.57%) 15	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 January 2013	Rationale/background for changes: - Revise the extent of safety review prior to the administration of the second vaccination at Month 6 (Part A2 phase of the trial). - Update the section on receipt of MMR and DTP vaccines at Month 12. - Correct that GSK study staff was not unblinded at the time of final analyses, but instead, was not blinded during the study at all; since it was a single blind study in which only subjects or parents/LARs were blinded, while the study staff was aware of the study treatment. - Add an additional blood pregnancy test as a country specific requirement for Panama. - Update the list of contributing authors.
05 December 2013	Rationale/background for changes: - Update the assay cut-offs used to measure the anti-HPV-16 and anti-HPV-18 antibody concentrations using the Enzyme-Linked ImmunoSorbent Assay (ELISA). The existing assays were replaced by the improved versions with new cut-offs. - Provision of HPV vaccination for subjects in Priorix + Infanrix group. - Revision of the scope of the second interim analysis to allow duly safety analysis during Part B enrolment. - Correct and modify text for a better clarification of study procedures with respect to laboratory testing, priority ranking, study vaccine preparation, etc. - Update the list of contributing authors.
07 July 2015	Rationale/background for changes: - Given the increasing success of adolescent immunisation programmes, the medical need for paediatric HPV vaccination (below 9 years of age) has become less clear. In addition, due to the measles vaccination campaigns in several countries related to the Pan American Health Organization (PAHO)/World Health Organization (WHO)-led measles elimination strategy, the subjects in the Latin American region who can be potentially enrolled in Part B of the study are few in number, apart from approximately 150 subjects who have already been enrolled in Part A of the study. As a result of this, further recruitment in Part B of the study that was planned initially has been stopped. The main change in the study design due to the cancellation of recruitment of subjects in Part B of the study is that the number of subjects has been reduced from approximately 1000 to approximately 150. The number of study groups has been changed from 4 groups to 2 groups. Consequent to the cancellation of Part B recruitment, the number of study objectives and endpoints initially planned in Protocol Amendment 2 were no longer achievable and has been amended in this Protocol Amendment 3. - The glossary of terms has been amended to remove the definitions of adequate contraception, menarche and menopause, and to update the definitions of blinding and medically significant conditions. - The list of assays has been updated. - Some references have been updated. - The indication for Cervarix has been updated. - The list of contributing authors has been updated, and some typographic errors have been corrected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported