Clinical trial results:
A phase IIIb, double-blind, randomized, controlled, multicentre study to assess the immunogenicity and safety of GlaxoSmithKline Biologicals' HPV-16/18 L1 AS04 vaccine administered intramuscularly according to a three-dose schedule (0, 1, 6 months) in healthy female subjects aged 10-25 years.

Summary

EudraCT number	2017-000416-42
Trial protocol	Outside EU/EEA
Global end of trial date	26 July 2010

Results information

Result version number	v1 (current)
This version publication date	14 February 2018
First version publication date	14 February 2018

Trial information

Trial identification

Sponsor protocol code	106069

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00481767
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 Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, 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	30 November 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 July 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To evaluate antibody responses enzyme-linked immunosorbent assay (ELISA) against HPV-16 and HPV-18 at Month 7 in subjects 15 - 25 years of age.
•To evaluate the antibody responses against HPV-16 and HPV-18 at Month 7 in subjects 10 - 14 years of age.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of vaccines, with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2007
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	Senegal: 342
Country: Number of subjects enrolled	Tanzania, United Republic of: 334
Worldwide total number of subjects	676
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)	232
Adolescents (12-17 years)	222
Adults (18-64 years)	222
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

At the screening visits, subjects were interviewed on their previous medical history (including smoking history, sexual and reproductive history and contraceptive status) and underwent general physical examination and pregnancy test.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Cervarix Group

Arm description:

Healthy female subjects who received 3 doses of Cervarix at Months 0, 1 and 6, administered intramuscularly into the deltoid region of the non-dominant arm. For some analyses the group was stratified by age into a 10-14 years of age group and a 15-25 years of age group.

Arm type	Active comparator
Investigational medicinal product name	Cervarix
Investigational medicinal product code	
Other name	GlaxoSmithKline Biologicals' HPV vaccine GSK580299; HPV-16/18 L1 AS04 vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of vaccine (0.5 mL) were administered intramuscularly into the deltoid region of the non-dominant arm, according to a 0, 1, 6-month schedule.

Arm title	Placebo Group

Arm description:

Healthy female subjects who received 3 doses of placebo at Months 0, 1 and 6, administered intramuscularly into the deltoid region of the non-dominant arm. For some analyses the group was stratified by age into a 10-14 years of age group and a 15-25 years of age group.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Al(OH)3
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of Placebo (0.5 mL) were administered intramuscularly into the deltoid region of the non-dominant arm, according to a 0, 1, 6-month schedule.

Number of subjects in period 1	Cervarix Group	Placebo Group
Started	450	226
Completed	418	205
Not completed	32	21
Consent withdrawn by subject	16	11
Lost to follow-up	16	10

Baseline characteristics

Reporting groups	
Reporting group title	Cervarix Group
Reporting group description:	
Healthy female subjects who received 3 doses of Cervarix at Months 0, 1 and 6, administered intramuscularly into the deltoid region of the non-dominant arm. For some analyses the group was stratified by age into a 10-14 years of age group and a 15-25 years of age group.	
Reporting group title	Placebo Group
Reporting group description:	
Healthy female subjects who received 3 doses of placebo at Months 0, 1 and 6, administered intramuscularly into the deltoid region of the non-dominant arm. For some analyses the group was stratified by age into a 10-14 years of age group and a 15-25 years of age group.	

Reporting group values	Cervarix Group	Placebo Group	Total
Number of subjects	450	226	676
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	16.9	16.8	
standard deviation	± 4.36	± 4.16	-
Gender categorical Units: Subjects			
Female	450	226	676
Male	0	0	0
Race/ethnicity Units: Subjects			
African/African american	431	219	650
Not specified	19	7	26

End points

End points reporting groups

Reporting group title	Cervarix Group
Reporting group description:	
Healthy female subjects who received 3 doses of Cervarix at Months 0, 1 and 6, administered intramuscularly into the deltoid region of the non-dominant arm. For some analyses the group was stratified by age into a 10-14 years of age group and a 15-25 years of age group.	
Reporting group title	Placebo Group
Reporting group description:	
Healthy female subjects who received 3 doses of placebo at Months 0, 1 and 6, administered intramuscularly into the deltoid region of the non-dominant arm. For some analyses the group was stratified by age into a 10-14 years of age group and a 15-25 years of age group.	

Primary: Number of seroconverted subjects for anti-human papillomavirus (HPV)-16 and 18 antibodies

End point title	Number of seroconverted subjects for anti-human papillomavirus (HPV)-16 and 18 antibodies[1]
End point description:	
A seroconverted subject was a subject with antibody titers below 8 or 7 Enzyme-linked Immunosorbent Assay Units per milliliter (EL.U/mL) for anti-HPV-16 and 18, respectively, before vaccination and antibody titers ≥ 8 or 7 EL.U/mL for anti-HPV-16 and 18, respectively, after vaccination. The groups were stratified by age for the analysis. The age strata were 10-14 years and 15-25 years.	
End point type	Primary
End point timeframe:	
At Month 7	

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: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	98		
Units: Subjects				
10-14 years anti-HPV-16 (N=130;59)	130	4		
15-25 years anti-HPV-16 (N=190;97)	190	5		
10-14 years anti-HPV-18 (N=128;56)	128	2		
15-25 years anti-HPV-18 (N=212;98)	212	5		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of anti-HPV-16 and anti-HPV-18 antibodies

End point title	Geometric Mean Titers (GMTs) of anti-HPV-16 and anti-HPV-18 antibodies[2]

End point description:

Titers were expressed as GMTs in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). The groups were stratified by age for the analysis. The age strata were 10-14 years and 15-25 years.

End point type	Primary

End point timeframe:

At Month 7

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: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237	114		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
10-14 years anti-HPV-16 (N=142;65)	18591.3 (16433.0 to 21033.1)	4.8 (4.2 to 5.5)		
15-25 years anti-HPV-16 (N=237;112)	10664.0 (9668.5 to 11762.0)	5.3 (4.6 to 6.1)		
10-14 years anti-HPV-18 (N=141;66)	6409.8 (5563.4 to 7385.0)	3.9 (3.6 to 4.2)		
15-25 years anti-HPV-18 (N=235;114)	3653.6 (3343.9 to 3991.9)	4.6 (4.0 to 5.3)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

A seroconverted subject was a subject with antibody titers below 8 or 7 Enzyme-linked Immunosorbent Assay Units per milliliter (EL.U/mL) for anti-HPV-16 and 18, respectively, before vaccination and antibody titers ≥ 8 or 7 EL.U/mL for anti-HPV-16 and 18, respectively, after vaccination. The groups were stratified by age for the analysis. The age strata were 10-14 years and 15-25 years.

End point type	Secondary

End point timeframe:

At Month 2 and Month 12

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	98		
Units: Subjects				
10-14 years anti-HPV-16 Month 2 (N=130;59)	130	1		
15-25 years anti-HPV-16 Month 2 (N=190;96)	190	3		
10-14 years anti-HPV-16 Month 12 (N=128;59)	128	2		
15-25 years anti-HPV-16 Month 12 (N=184;94)	184	7		
10-14 years anti-HPV-18 Month 2 (N=128;55)	128	1		
15-25 years anti-HPV-18 Month 2 (N=212;98)	212	4		
10-14 years anti-HPV-18 Month 12 (N=126;56)	125	0		
15-25 years anti-HPV-18 Month 12 (N=205;96)	205	6		

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs for anti-HPV-16 and anti-HPV-18 antibodies

End point title	GMTs for anti-HPV-16 and anti-HPV-18 antibodies

End point description:

Titers were expressed as GMTs in Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). The groups were stratified by age for the analysis. The age strata were 10-14 years and 15-25 years.

End point type	Secondary

End point timeframe:

At Month 2 and Month 12

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237	112		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
10-14 years anti-HPV-16 Month 2 (N=142;64)	5340.2 (4823.7 to 5912.0)	4.5 (4.0 to 5.0)		
15-25 years anti-HPV-16 Month 2 (N=237;112)	3732.6 (3436.6 to 4054.1)	4.9 (4.3 to 5.5)		
10-14 years anti-HPV-16 Month 12 (N=139;65)	4016.2 (3323.3 to 4853.7)	4.7 (4.2 to 5.3)		

15-25 years anti-HPV-16 Month 12 (N=229;109)	2464.2 (2196.5 to 2764.5)	5.6 (4.7 to 6.6)		
10-14 years anti-HPV-18 Month 2 (N=141;65)	3016.7 (2677.4 to 3398.9)	3.9 (3.6 to 4.3)		
15-25 years anti-HPV-18 Month 2 (N=235;112)	2039.3 (1861.3 to 2234.4)	4.6 (4.0 to 5.3)		
10-14 years anti-HPV-18 Month 12 (N=138;66)	1422.1 (1170.0 to 1728.4)	3.7 (3.5 to 3.9)		
15-25 years anti-HPV-18 Month 12 (N=227;111)	855.9 (768.3 to 953.5)	4.6 (4.0 to 5.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: 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

End point description:

Solicited local symptoms assessed were pain and swelling at the injection site. Any = occurrence of any solicited local symptom regardless of their intensity grade. Grade 3 swelling = swelling spreading beyond 50 millimeters (mm) of injection site. Grade 3 pain = pain that prevented normal activity.

End point type	Secondary

End point timeframe:

Within 7 days (Day 0-6) after each dose and across doses

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	450	226		
Units: Subjects				
Any Pain, Dose 1 (N=450;226)	309	116		
Grade 3 Pain, Dose 1 (N=450;226)	2	0		
Any Swelling, Dose 1 (N=450;226)	15	7		
Grade 3 Swelling, Dose 1 (N=450;226)	0	0		
Any Pain, Dose 2 (N=437;217)	265	95		
Grade 3 Pain, Dose 2 (N=437;217)	0	0		
Any Swelling, Dose 2 (N=437;217)	45	15		
Grade 3 Swelling, Dose 2 (N=437;217)	0	0		
Any Pain, Dose 3 (N=411;200)	200	66		
Grade 3 Pain, Dose 3 (N=411;200)	0	0		
Any Swelling, Dose 3 (N=411;200)	26	10		
Grade 3 Swelling, Dose 3 (N=411;200)	0	0		
Any Pain, Across doses (N=450;226)	375	166		
Grade 3 Pain, Across doses (N=450;226)	2	0		

Any Swelling, Across doses (N=450;226)	74	27		
Grade 3 Swelling, Across doses (N=450;226)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: 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

End point description:

Solicited general symptoms assessed were arthralgia (only joints that are distal from the injection site), fatigue, fever (defined as axillary temperature ≥ 37.5 degrees Celsius), gastrointestinal symptoms, headache, myalgia, rash and urticaria. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 urticaria = urticaria distributed on at least 4 body areas. Grade 3 fever = axillary temperature > 39.0 °C. Related = symptom assessed by the investigator as causally related to the study vaccination.

End point type	Secondary

End point timeframe:

Within 7 days (Day 0-6) after each dose and across doses

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	450	226		
Units: Subjects				
Any Arthralgia, Dose 1 (N=450;226)	19	10		
Grade 3 Arthralgia, Dose 1 (N=450;226)	0	0		
Related Arthralgia, Dose 1 (N=450;226)	7	2		
Any Fatigue, Dose 1 (N=450;226)	34	12		
Grade 3 Fatigue, Dose 1 (N=450;226)	0	0		
Related Fatigue, Dose 1 (N=450;226)	21	3		
Any Fever, Dose 1 (N=450;226)	72	43		
Grade 3 Fever, Dose 1 (N=450;226)	0	0		
Related Fever, Dose 1 (N=450;226)	34	17		
Any Gastrointestinal, Dose 1 (N=450;226)	34	21		
Grade 3 Gastrointestinal, Dose 1 (N=450;226)	0	0		
Related Gastrointestinal, Dose 1 (N=450;226)	14	8		
Any Headache, Dose 1 (N=450;226)	89	56		
Grade 3 Headache, Dose 1 (N=450;226)	0	0		
Related Headache, Dose 1 (N=450;226)	51	25		
Any Myalgia, Dose 1 (N=450;226)	35	16		
Grade 3 Myalgia, Dose 1 (N=450;226)	0	0		

Related Myalgia, Dose 1 (N=450;226)	22	7		
Any Rash, Dose 1 (N=450;226)	14	8		
Grade 3 Rash, Dose 1 (N=450;226)	0	0		
Related Rash, Dose 1 (N=450;226)	1	0		
Any Urticaria, Dose 1 (N=450;226)	12	7		
Grade 3 Urticaria, Dose 1 (N=450;226)	0	0		
Related Urticaria, Dose 1 (N=450;226)	0	0		
Any Arthralgia, Dose 2 (N=437;217)	47	17		
Grade 3 Arthralgia, Dose 2 (N=437;217)	0	0		
Related Arthralgia, Dose 2 (N=437;217)	4	2		
Any Fatigue, Dose 2 (N=437;217)	62	25		
Grade 3 Fatigue, Dose 2 (N=437;217)	0	0		
Related Fatigue, Dose 2 (N=437;217)	17	4		
Any Fever, Dose 2 (N=437;217)	82	33		
Grade 3 Fever, Dose 2 (N=437;217)	0	0		
Related Fever, Dose 2 (N=437;217)	19	8		
Any Gastrointestinal, Dose 2 (N=437;217)	66	26		
Grade 3 Gastrointestinal, Dose 2 (N=437;217)	0	0		
Related Gastrointestinal, Dose 2 (N=437;217)	15	6		
Any Headache, Dose 2 (N=437;217)	96	49		
Grade 3 Headache, Dose 2 (N=437;217)	0	0		
Related Headache, Dose 2 (N=437;217)	40	18		
Any Myalgia, Dose 2 (N=437;217)	50	17		
Grade 3 Myalgia, Dose 2 (N=437;217)	0	0		
Related Myalgia, Dose 2 (N=437;217)	9	3		
Any Rash, Dose 2 (N=437;217)	44	15		
Grade 3 Rash, Dose 2 (N=437;217)	0	0		
Related Rash, Dose 2 (N=437;217)	1	0		
Any Urticaria, Dose 2 (N=437;217)	43	14		
Grade 3 Urticaria, Dose 2 (N=437;217)	0	0		
Related Urticaria, Dose 2 (N=437;217)	0	0		
Any Arthralgia, Dose 3 (N=411;200)	28	10		
Grade 3 Arthralgia, Dose 3 (N=411;200)	0	0		
Related Arthralgia, Dose 3 (N=411;200)	0	0		
Any Fatigue, Dose 3 (N=411;200)	34	13		
Grade 3 Fatigue, Dose 3 (N=411;200)	0	0		
Related Fatigue, Dose 3 (N=411;200)	4	3		
Any Fever, Dose 3 (N=411;200)	81	33		
Grade 3 Fever, Dose 3 (N=411;200)	0	0		
Related Fever, Dose 3 (N=411;200)	20	9		
Any Gastrointestinal, Dose 3 (N=411;200)	43	19		
Grade 3 Gastrointestinal, Dose 3 (N=411;200)	0	0		
Related Gastrointestinal, Dose 3 (N=411;200)	5	5		
Any Headache, Dose 3 (N=411;200)	71	33		
Grade 3 Headache, Dose 3 (N=411;200)	0	0		

Related Headache, Dose 3 (N=411;200)	22	12		
Any Myalgia, Dose 3 (N=411;200)	28	10		
Grade 3 Myalgia, Dose 3 (N=411;200)	0	0		
Related Myalgia, Dose 3 (N=411;200)	1	0		
Any Rash, Dose 3 (N=411;200)	26	12		
Grade 3 Rash, Dose 3 (N=411;200)	0	0		
Related Rash, Dose 3 (N=411;200)	0	0		
Any Urticaria, Dose 3 (N=411;200)	26	11		
Grade 3 Urticaria, Dose 3 (N=411;200)	0	0		
Related Urticaria, Dose 3 (N=411;200)	0	0		
Any Arthralgia, Across doses (N=450;226)	77	32		
Grade 3 Arthralgia, Across doses (N=450;226)	0	0		
Related Arthralgia, Across doses (N=450;226)	10	4		
Any Fatigue, Across doses (N=450;226)	111	42		
Grade 3 Fatigue, Across doses (N=450;226)	0	0		
Related Fatigue, Across doses (N=450;226)	39	9		
Any Fever, Across doses (N=450;226)	147	70		
Grade 3 Fever, Across doses (N=450;226)	0	0		
Related Fever, Across doses (N=450;226)	57	27		
Any Gastrointestinal, Across doses (N=450;226)	118	56		
Grade 3 Gastrointestinal, Across doses(N=450;226)	0	0		
Related Gastrointestinal, Across doses(N=450;226)	31	17		
Any Headache, Across doses (N=450;226)	189	109		
Grade 3 Headache, Across doses (N=450;226)	0	0		
Related Headache, Across doses (N=450;226)	101	46		
Any Myalgia, Across doses (N=450;226)	90	36		
Grade 3 Myalgia, Across doses (N=450;226)	0	0		
Related Myalgia, Across doses (N=450;226)	27	9		
Any Rash, Across doses (N=450;226)	71	30		
Grade 3 Rash, Across doses (N=450;226)	0	0		
Related Rash, Across doses (N=450;226)	2	0		
Any Urticaria, Across doses (N=450;226)	68	27		
Grade 3 Urticaria, Across doses (N=450;226)	0	0		
Related Urticaria, Across doses (N=450;226)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related unsolicited adverse events (AEs)

End point title	Number of subjects with any, grade 3 and related unsolicited adverse events (AEs)

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 = any unsolicited AE regardless of intensity and relationship to vaccination. Grade 3 = an unsolicited AE that prevented normal everyday activity. Related = unsolicited AE assessed by the investigator as causally related to the study vaccination.

End point type	Secondary

End point timeframe:

Within 30 days (Day 0-29) after any vaccination

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	450	226		
Units: Subjects				
Any AE(s)	235	142		
Grade 3 AE(s)	5	1		
Related AE(s)	3	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with new onset of chronic diseases (NOCDs) and medically significant conditions (MSCs)

End point title	Number of subjects with new onset of chronic diseases (NOCDs) and medically significant conditions (MSCs)

End point description:

NOCDs assessed included autoimmune disorders, asthma, type I diabetes, allergies. MSCs assessed included AEs prompting emergency room or physician visits that were not related to common diseases or routine visits for physical examination or vaccination, or serious adverse events (SAEs) that were not related to common diseases. Common diseases included 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 Day 0 up to Month 7 and from Month 7 up to Month 12

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	450	226		
Units: Subjects				
NOCD(s) up to Month 7 (N=450;226)	10	8		
NOCD(s) Month 7-12 (N=421;208)	1	3		
MSC(s) up to Month 7 (N=450;226)	289	161		
MSC(s) Month 7-12 (N=421;208)	121	68		

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:

SAEs assessed included medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or were 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 7 and from Month 7 up to Month 12

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	450	226		
Units: Subjects				
Up to Month 7	12	10		
Up to Month 12	17	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with pregnancies and their outcomes

End point title	Number of subjects with pregnancies and their outcomes

End point description:

Pregnancy outcomes were ectopic pregnancy, elective termination no apparent congenital anomaly, live infant no apparent congenital anomaly, premature live infant no apparent congenital anomaly, lost to follow-up and spontaneous abortion no apparent congenital anomaly.

End point type	Secondary

End point timeframe:

From Day 0 up to Month 12

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	10		
Units: Subjects				
Ectopic pregnancy	1	0		
Elective termination	3	3		
Live infant	5	5		
Premature live infant	3	1		
Lost to follow-up	1	0		
Spontaneous abortion	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Senegalese subjects with clinically relevant abnormalities in parameters assessed

End point title	Number of Senegalese subjects with clinically relevant abnormalities in parameters assessed

End point description:

Biochemical and haematological parameters assessed were:
Alanine amino-transferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), hematocrit (HC), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC), white blood cells (WBC).
Number of subjects were separated with respect to their results at pre-vaccination, i.e. whether their results were in, above or below the normal range.
N for each category at pre-vaccination noted in category title. For each parameter and for each range it was assessed whether the values of the subjects were in, above or below the normal range.

End point type	Secondary

End point timeframe:

At Month 7

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	105		
Units: Subjects				
ALT, pre-vacc. ABOVE (N=8;4), Month 7 NORMAL	7	4		
ALT, pre-vacc.ABOVE (N=8;4), Month 7 BELOW	0	0		
ALT, pre-vacc. ABOVE (N=8;4), Month 7 ABOVE	1	0		
ALT, pre-vacc. BELOW (N=39;17), Month 7 NORMAL	15	7		
ALT, pre-vacc. BELOW (N=39;17), Month 7 BELOW	24	10		

ALT, pre-vacc. BELOW (N=39;17), Month 7 ABOVE	0	0		
ALT, pre-vacc. NORMAL (N=170;84), Month 7 NORMAL	137	57		
ALT, pre-vacc. NORMAL (N=170;84), Month 7 BELOW	30	25		
ALT, pre-vacc. NORMAL (N=170;84), Month 7 ABOVE	3	2		
BAS, pre-vacc. NORMAL (N=217;105), Month 7 NORMAL	216	105		
BAS, pre-vacc. NORMAL (N=217;105), Month 7 BELOW	0	0		
BAS, pre-vacc. NORMAL (N=217;105), Month 7 ABOVE	1	0		
CREA, pre-vacc. ABOVE (N=2;1), Month 7 NORMAL	1	1		
CREA, pre-vacc. ABOVE (N=2;1), Month 7 BELOW	0	0		
CREA, pre-vacc. ABOVE (N=2;1), Month 7 ABOVE	1	0		
CREA, pre-vacc. BELOW (N=56;30), Month 7 NORMAL	19	13		
CREA, pre-vacc. BELOW (N=56;30), Month 7 BELOW	37	17		
CREA, pre-vacc. BELOW (N=56;30), Month 7 ABOVE	0	0		
CREA, pre-vacc. NORMAL (N=159;74), Month 7 NORMAL	149	68		
CREA, pre-vacc. NORMAL (N=159;74), Month 7 BELOW	10	4		
CREA, pre-vacc. NORMAL (N=159;74), Month 7 ABOVE	0	2		
EOS, pre-vacc. ABOVE (N=43;28), Month 7 NORMAL	9	12		
EOS, pre-vacc. ABOVE (N=43;28), Month 7 BELOW	0	0		
EOS, pre-vacc. ABOVE (N=43;28), Month 7 ABOVE	34	16		
EOS, pre-vacc. BELOW (N=19;10), Month 7 NORMAL	17	9		
EOS, pre-vacc. BELOW (N=19;10), Month 7 BELOW	2	1		
EOS, pre-vacc. BELOW (N=19;10), Month 7 ABOVE	0	0		
EOS, pre-vacc. NORMAL (N=155;67), Month 7 NORMAL	134	56		
EOS, pre-vacc. NORMAL (N=155;67), Month 7 BELOW	3	2		
EOS, pre-vacc. NORMAL (N=155;67), Month 7 ABOVE	18	9		
HC, pre-vacc. BELOW (N=75;33), Month 7 NORMAL	16	7		
HC, pre-vacc. BELOW (N=75;33), Month 7 BELOW	59	26		
HC, pre-vacc. BELOW (N=75;33), Month 7 ABOVE	0	0		
HC, pre-vacc. NORMAL (N=142;72), Month 7 NORMAL	104	52		
HC, pre-vacc. NORMAL (N=142;72), Month 7 BELOW	38	20		
HC, pre-vacc. NORMAL (N=142;72), Month 7 ABOVE	0	0		

LYM, pre-vacc. ABOVE (N=77;41), Month 7 NORMAL	23	11		
LYM, pre-vacc. ABOVE (N=77;41), Month 7 BELOW	4	3		
LYM, pre-vacc. ABOVE (N=77;41), Month 7 ABOVE	50	27		
LYM, pre-vacc. BELOW (N=41;19), Month 7 NORMAL	23	8		
LYM, pre-vacc. BELOW (N=41;19), Month 7 BELOW	11	6		
LYM, pre-vacc. BELOW (N=41;19), Month 7 ABOVE	7	5		
LYM, pre-vacc. NORMAL (N=99;45), Month 7 NORMAL	47	19		
LYM, pre-vacc. NORMAL (N=99;45), Month 7 BELOW	17	2		
LYM, pre-vacc. NORMAL (N=99;45), Month 7 ABOVE	35	24		
MON, pre-vacc. ABOVE (N=48;35), Month 7 NORMAL	17	4		
MON, pre-vacc. ABOVE (N=48;35), Month 7 BELOW	0	0		
MON, pre-vacc. ABOVE (N=48;35), Month 7 ABOVE	31	31		
MON, pre-vacc. NORMAL (N=169;70), Month 7 NORMAL	108	45		
MON, pre-vacc. NORMAL (N=169;70), Month 7 BELOW	0	0		
MON, pre-vacc. NORMAL (N=169;70), Month 7 ABOVE	61	25		
NEU, pre-vacc. ABOVE (N=8;3), Month 7 NORMAL	0	0		
NEU, pre-vacc. ABOVE (N=8;3), Month 7 BELOW	7	3		
NEU, pre-vacc. ABOVE (N=8;3), Month 7 ABOVE	1	0		
NEU, pre-vacc. BELOW (N=176;91), Month 7 NORMAL	9	4		
NEU, pre-vacc. BELOW (N=176;91), Month 7 BELOW	165	86		
NEU, pre-vacc. BELOW (N=176;91), Month 7 ABOVE	2	1		
NEU, pre-vacc. NORMAL (N=33;11), Month 7 NORMAL	4	1		
NEU, pre-vacc. NORMAL (N=33;11), Month 7 BELOW	26	10		
NEU, pre-vacc. NORMAL (N=33;11), Month 7 ABOVE	3	0		
PLA, pre-vacc. ABOVE (N=17;6), Month 7 NORMAL	10	4		
PLA, pre-vacc. ABOVE (N=17;6), Month 7 BELOW	0	0		
PLA, pre-vacc. ABOVE (N=17;6), Month 7 ABOVE	7	2		
PLA. pre-vacc. BELOW (N=2;3), Month 7 NORMAL	1	0		
PLA. pre-vacc. BELOW (N=2;3), Month 7 BELOW	1	2		
PLA. pre-vacc. BELOW (N=2;3), Month 7 ABOVE	0	1		
PLA, pre-vacc. NORMAL (N=198;96), Month 7 NORMAL	194	96		

PLA, pre-vacc. NORMAL (N=198;96), Month 7 BELOW	0	0		
PLA, pre-vacc. NORMAL (N=198;96), Month 7 ABOVE	4	0		
RBC, pre-vacc. BELOW (N=29;11), Month 7 NORMAL	10	3		
RBC, pre-vacc. BELOW (N=29;11), Month 7 BELOW	19	8		
RBC, pre-vacc. BELOW (N=29;11), Month 7 ABOVE	0	0		
RBC, pre-vacc. NORMAL (N=188;94), Month 7 NORMAL	176	89		
RBC, pre-vacc. NORMAL (N=188;94), Month 7 BELOW	12	5		
RBC, pre-vacc. NORMAL (N=188;94), Month 7 ABOVE	0	0		
WBC, pre-vacc. ABOVE (N=9;7), Month 7 NORMAL	6	6		
WBC, pre-vacc. ABOVE (N=9;7), Month 7 BELOW	0	0		
WBC, pre-vacc. ABOVE (N=9;7), Month 7 ABOVE	3	1		
WBC, pre-vacc. BELOW (N=21;12), Month 7 NORMAL	5	6		
WBC, pre-vacc. BELOW (N=21;12), Month 7 BELOW	16	6		
WBC, pre-vacc. BELOW (N=21;12), Month 7 ABOVE	0	0		
WBC, pre-vacc. NORMAL (N=187;86), Month 7 NORMAL	158	72		
WBC, pre-vacc. NORMAL (N=187;86), Month 7 BELOW	26	13		
WBC, pre-vacc. NORMAL (N=187;86), Month 7 ABOVE	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Tanzanian subjects with clinically relevant abnormalities in parameters assessed

End point title	Number of Tanzanian subjects with clinically relevant abnormalities in parameters assessed

End point description:

Biochemical and haematological parameters assessed were:
Alanine amino-transferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), hematocrit (HC), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC), white blood cells (WBC).
Number of subjects were separated with respect to their results at pre-vaccination, i.e. whether their results were in, above or below the normal range.
N for each category at pre-vaccination noted in category title. For each parameter and for each range it was assessed whether the values of the subjects were in, above or below the normal range.

End point type	Secondary

End point timeframe:

At Month 7

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	187	96		
Units: Subjects				
ALT, pre-vacc. ABOVE (N=3;3), Month 7 NORMAL	2	2		
ALT, pre-vacc. ABOVE (N=3;3), Month 7 BELOW	0	1		
ALT, pre-vacc. ABOVE (N=3;3), Month 7 ABOVE	1	0		
ALT, pre-vacc. BELOW (N=13;11), Month 7 NORMAL	7	3		
ALT, pre-vacc. BELOW (N=13;11), Month 7 BELOW	6	8		
ALT, pre-vacc. BELOW (N=13;11), Month 7 ABOVE	0	0		
ALT, pre-vacc. NORMAL (N=183;85), Month 7 NORMAL	144	65		
ALT, pre-vacc. NORMAL (N=183;85), Month 7 BELOW	39	20		
ALT, pre-vacc. NORMAL (N=183;85), Month 7 ABOVE	0	0		
BAS, pre-vacc. ABOVE (N=21;12), Month 7 NORMAL	19	12		
BAS, pre-vacc. ABOVE (N=21;12), Month 7 BELOW	0	0		
BAS, pre-vacc. ABOVE (N=21;12), Month 7 ABOVE	2	0		
BAS, pre-vacc. NORMAL (N=178;87), Month 7 NORMAL	163	81		
BAS, pre-vacc. NORMAL (N=178;87), Month 7 BELOW	0	0		
BAS, pre-vacc. NORMAL (N=178;87), Month 7 ABOVE	15	6		
CREA, pre-vacc. BELOW (N=43;14), Month 7 NORMAL	2	2		
CREA, pre-vacc. BELOW (N=43;14), Month 7 BELOW	41	12		
CREA, pre-vacc. BELOW (N=43;14), Month 7 ABOVE	0	0		
CREA, pre-vacc. NORMAL (N=156;85), Month 7 NORMAL	40	14		
CREA, pre-vacc. NORMAL (N=156;85), Month 7 BELOW	116	71		
CREA, pre-vacc. NORMAL (N=156;85), Month 7 ABOVE	0	0		
EOS, pre-vacc. ABOVE (N=76;39), Month 7 NORMAL	14	4		
EOS, pre-vacc. ABOVE (N=76;39), Month 7 BELOW	0	0		
EOS, pre-vacc. ABOVE (N=76;39), Month 7 ABOVE	61	35		
EOS, pre-vacc. ABOVE (N=76;39), Month 7 MISSING	1	0		
EOS, pre-vacc. NORMAL (N=123;60), Month 7 NORMAL	92	52		

EOS, pre-vacc. NORMAL (N=123;60), Month 7 BELOW	0	0		
EOS, pre-vacc. NORMAL (N=123;60), Month 7 ABOVE	31	8		
HC, pre-vacc. ABOVE (N=1;0), Month 7 NORMAL	1	0		
HC, pre-vacc. ABOVE (N=1;0), Month 7 BELOW	0	0		
HC, pre-vacc. ABOVE (N=1;0), Month 7 ABOVE	0	0		
HC, pre-vacc. BELOW (N=60;35), Month 7 NORMAL	20	6		
HC, pre-vacc. BELOW (N=60;35), Month 7 BELOW	40	29		
HC, pre-vacc. BELOW (N=60;35), Month 7 ABOVE	0	0		
HC, pre-vacc. NORMAL (N=138;64), Month 7 NORMAL	118	51		
HC, pre-vacc. NORMAL (N=138;64), Month 7 BELOW	20	13		
HC, pre-vacc. NORMAL (N=138;64), Month 7 ABOVE	0	0		
LYM, pre-vacc. ABOVE (N=20;8), Month 7 NORMAL	12	7		
LYM, pre-vacc. ABOVE (N=20;8), Month 7 BELOW	0	0		
LYM, pre-vacc. ABOVE (N=20;8), Month 7 ABOVE	8	1		
LYM, pre-vacc. NORMAL (N=179;91), Month 7 NORMAL	166	81		
LYM, pre-vacc. NORMAL (N=179;91), Month 7 BELOW	3	0		
LYM, pre-vacc. NORMAL (N=179;91), Month 7 ABOVE	10	10		
MON, pre-vacc. ABOVE (N=12;7), Month 7 NORMAL	6	6		
MON, pre-vacc. ABOVE (N=12;7), Month 7 BELOW	0	0		
MON, pre-vacc. ABOVE (N=12;7), Month 7 ABOVE	6	1		
MON, pre-vacc. NORMAL (N=187;92), Month 7 NORMAL	180	85		
MON, pre-vacc. NORMAL (N=187;92), Month 7 BELOW	0	0		
MON, pre-vacc. NORMAL (N=187;92), Month 7 ABOVE	7	7		
NEU, pre-vacc. BELOW (N=36;16), Month 7 NORMAL	13	9		
NEU, pre-vacc. BELOW (N=36;16), Month 7 BELOW	22	7		
NEU, pre-vacc. BELOW (N=36;16), Month 7 ABOVE	0	0		
NEU, pre-vacc. BELOW (N=36;16), Month 7 MISSING	1	0		
NEU, pre-vacc. NORMAL (N=163;83), Month 7 NORMAL	145	70		
NEU, pre-vacc. NORMAL (N=163;83), Month 7 BELOW	17	13		
NEU, pre-vacc. NORMAL (N=163;83), Month 7 ABOVE	1	0		
PLA, pre-vacc. ABOVE (N=10;3), Month 7 NORMAL	7	1		

PLA, pre-vacc. ABOVE (N=10;3), Month 7 BELOW	0	0		
PLA, pre-vacc. ABOVE (N=10;3), Month 7 ABOVE	3	2		
PLA, pre-vacc. BELOW (N=5;0), Month 7 NORMAL	4	0		
PLA, pre-vacc. BELOW (N=5;0), Month 7 BELOW	1	0		
PLA, pre-vacc. BELOW (N=5;0), Month 7 ABOVE	0	0		
PLA, pre-vacc. NORMAL (N=184;96), Month 7 NORMAL	180	92		
PLA, pre-vacc. NORMAL (N=184;96), Month 7 BELOW	2	0		
PLA, pre-vacc. NORMAL (N=184;96), Month 7 ABOVE	2	4		
RBC, pre-vacc. ABOVE (N=11;7), Month 7 NORMAL	6	4		
RBC, pre-vacc. ABOVE (N=11;7), Month 7 BELOW	0	0		
RBC, pre-vacc. ABOVE (N=11;7), Month 7 ABOVE	5	3		
RBC, pre-vacc. BELOW (N=2;1), Month 7 NORMAL	1	0		
RBC, pre-vacc. BELOW (N=2;1), Month 7 BELOW	1	1		
RBC, pre-vacc. BELOW (N=2;1), Month 7 ABOVE	0	0		
RBC, pre-vacc. NORMAL (N=186;91), Month 7 NORMAL	177	90		
RBC, pre-vacc. NORMAL (N=186;91), Month 7 BELOW	5	0		
RBC, pre-vacc. NORMAL (N=186;91), Month 7 ABOVE	4	1		
WBC, pre-vacc. ABOVE (N=17;7), Month 7 NORMAL	13	6		
WBC, pre-vacc. ABOVE (N=17;7), Month 7 BELOW	0	0		
WBC, pre-vacc. ABOVE (N=17;7), Month 7 ABOVE	4	1		
WBC, pre-vacc. BELOW (N=0;2), Month 7 NORMAL	0	2		
WBC, pre-vacc. BELOW (N=0;2), Month 7 BELOW	0	0		
WBC, pre-vacc. BELOW (N=0;2), Month 7 ABOVE	0	0		
WBC, pre-vacc. NORMAL (N=182;90), Month 7 NORMAL	177	86		
WBC, pre-vacc. NORMAL (N=182;90), Month 7 BELOW	4	2		
WBC, pre-vacc. NORMAL (N=182;90), Month 7 ABOVE	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Senegalese subjects with clinically relevant abnormalities in

parameters assessed

End point title	Number of Senegalese subjects with clinically relevant abnormalities in parameters assessed

End point description:

Biochemical and haematological parameters assessed were:
Alanine amino-transferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), hematocrit (HC), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC), white blood cells (WBC).
Number of subjects were separated with respect to their results at pre-vaccination, i.e. whether their results were in, above or below the normal range.
N for each category at pre-vaccination noted in category title. For each parameter and for each range it was assessed whether the values of the subjects were in, above or below the normal range.

End point type	Secondary

End point timeframe:

At Month 12

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	102		
Units: Subjects				
ALT, pre-vacc. ABOVE (N=8;4), Month 12 NORMAL	8	4		
ALT, pre-vacc.ABOVE (N=8;4), Month 12 BELOW	0	0		
ALT, pre-vacc. ABOVE (N=8;4), Month 12 ABOVE	0	0		
ALT, pre-vacc. BELOW (N=38;17), Month 12 NORMAL	17	9		
ALT, pre-vacc. BELOW (N=38;17), Month 12 BELOW	21	8		
ALT, pre-vacc. BELOW (N=38;17), Month 12 ABOVE	0	0		
ALT, pre-vacc. NORMAL (N=165;81), Month 12 NORMAL	139	61		
ALT, pre-vacc. NORMAL (N=165;81), Month 12 BELOW	24	17		
ALT, pre-vacc. NORMAL (N=165;81), Month 12 ABOVE	2	3		
BAS, pre-vacc. NORMAL (N=211;102), Month 12 NORMAL	210	102		
BAS, pre-vacc. NORMAL (N=211;102), Month 12 BELOW	0	0		
BAS, pre-vacc. NORMAL (N=211;102), Month 12 ABOVE	1	0		
CREA, pre-vacc. ABOVE (N=2;1), Month 12 NORMAL	1	0		
CREA, pre-vacc. ABOVE (N=2;1), Month 12 BELOW	0	1		
CREA, pre-vacc. ABOVE (N=2;1), Month 12 ABOVE	1	0		
CREA, pre-vacc. BELOW (N=56;29), Month 12 NORMAL	13	6		
CREA, pre-vacc. BELOW (N=56;29), Month 12 BELOW	43	23		
CREA, pre-vacc. BELOW (N=56;29), Month 12 ABOVE	0	0		

CREA, pre-vacc. NORMAL (N=153;72), Month 12 NORMAL	130	64		
CREA, pre-vacc. NORMAL (N=153;72), Month 12 BELOW	23	8		
CREA, pre-vacc. NORMAL (N=153;72), Month 12 ABOVE	0	0		
EOS, pre-vacc. ABOVE (N=43;28), Month 12 NORMAL	14	11		
EOS, pre-vacc. ABOVE (N=43;28), Month 12 BELOW	1	0		
EOS, pre-vacc. ABOVE (N=43;28), Month 12 ABOVE	28	17		
EOS, pre-vacc. BELOW (N=19;10), Month 12 NORMAL	13	6		
EOS, pre-vacc. BELOW (N=19;10), Month 12 BELOW	6	3		
EOS, pre-vacc. BELOW (N=19;10), Month 12 ABOVE	0	1		
EOS, pre-vacc. NORMAL (N=149;64), Month 12 NORMAL	126	52		
EOS, pre-vacc. NORMAL (N=149;64), Month 12 BELOW	6	2		
EOS, pre-vacc. NORMAL (N=149;64), Month 12 ABOVE	17	10		
HC, pre-vacc. BELOW (N=71;33), Month 12 NORMAL	15	10		
HC, pre-vacc. BELOW (N=71;33), Month 12 BELOW	56	23		
HC, pre-vacc. BELOW (N=71;33), Month 12 ABOVE	0	0		
HC, pre-vacc. NORMAL (N=140;69), Month 12 NORMAL	108	45		
HC, pre-vacc. NORMAL (N=140;69), Month 12 BELOW	32	24		
HC, pre-vacc. NORMAL (N=140;69), Month 12 ABOVE	0	0		
LYM, pre-vacc. ABOVE (N=75;41), Month 12 NORMAL	24	16		
LYM, pre-vacc. ABOVE (N=75;41), Month 12 BELOW	4	3		
LYM, pre-vacc. ABOVE (N=75;41), Month 12 ABOVE	47	22		
LYM, pre-vacc. BELOW (N=38;19), Month 12 NORMAL	9	8		
LYM, pre-vacc. BELOW (N=38;19), Month 12 BELOW	15	5		
LYM, pre-vacc. BELOW (N=38;19), Month 12 ABOVE	14	6		
LYM, pre-vacc. NORMAL (N=98;42), Month 12 NORMAL	48	24		
LYM, pre-vacc. NORMAL (N=98;42), Month 12 BELOW	27	4		
LYM, pre-vacc. NORMAL (N=98;42), Month 12 ABOVE	23	14		
MON, pre-vacc. ABOVE (N=45;34), Month 12 NORMAL	13	10		
MON, pre-vacc. ABOVE (N=45;34), Month 12 BELOW	0	0		
MON, pre-vacc. ABOVE (N=45;34), Month 12 ABOVE	32	24		
MON, pre-vacc. NORMAL (N=166;68), Month 12 NORMAL	102	38		

MON, pre-vacc. NORMAL (N=166;68), Month 12 BELOW	0	0		
MON, pre-vacc. NORMAL (N=166;68), Month 12 ABOVE	64	30		
NEU, pre-vacc. ABOVE (N=8;3), Month 12 NORMAL	4	0		
NEU, pre-vacc. ABOVE (N=8;3), Month 12 BELOW	4	3		
NEU, pre-vacc. ABOVE (N=8;3), Month 12 ABOVE	0	0		
NEU, pre-vacc. BELOW (N=173;88), Month 12 NORMAL	11	5		
NEU, pre-vacc. BELOW (N=173;88), Month 12 BELOW	160	83		
NEU, pre-vacc. BELOW (N=173;88), Month 12 ABOVE	2	0		
NEU, pre-vacc. NORMAL (N=30;11), Month 12 NORMAL	7	1		
NEU, pre-vacc. NORMAL (N=30;11), Month 12 BELOW	22	9		
NEU, pre-vacc. NORMAL (N=30;11), Month 12 ABOVE	1	1		
PLA, pre-vacc. ABOVE (N=17;6), Month 12 NORMAL	13	4		
PLA, pre-vacc. ABOVE (N=17;6), Month 12 BELOW	0	0		
PLA, pre-vacc. ABOVE (N=17;6), Month 12 ABOVE	4	2		
PLA. pre-vacc. BELOW (N=2;3), Month 12 NORMAL	1	1		
PLA. pre-vacc. BELOW (N=2;3), Month 12 BELOW	1	2		
PLA. pre-vacc. BELOW (N=2;3), Month 12 ABOVE	0	0		
PLA, pre-vacc. NORMAL (N=192;93), Month 12 NORMAL	188	93		
PLA, pre-vacc. NORMAL (N=198;93), Month 12 BELOW	3	0		
PLA, pre-vacc. NORMAL (N=198;93), Month 12 ABOVE	1	0		
RBC, pre-vacc. BELOW (N=27;11), Month 12 NORMAL	8	5		
RBC, pre-vacc. BELOW (N=27;11), Month 12 BELOW	19	6		
RBC, pre-vacc. BELOW (N=27;11), Month 12 ABOVE	0	0		
RBC, pre-vacc. NORMAL (N=184;91), Month 12 NORMAL	169	80		
RBC, pre-vacc. NORMAL (N=184;91), Month 12 BELOW	15	11		
RBC, pre-vacc. NORMAL (N=184;91), Month 12 ABOVE	0	0		
WBC, pre-vacc. ABOVE (N=8;7), Month 12 NORMAL	6	7		
WBC, pre-vacc. ABOVE (N=8;7), Month 12 BELOW	0	0		
WBC, pre-vacc. ABOVE (N=8;7), Month 12 ABOVE	2	0		
WBC, pre-vacc. BELOW (N=19;12), Month 12 NORMAL	10	5		
WBC, pre-vacc. BELOW (N=19;12), Month 12 BELOW	9	7		

WBC, pre-vacc. BELOW (N=19;12), Month 12 ABOVE	0	0		
WBC, pre-vacc. NORMAL (N=184;83), Month 12 NORMAL	156	64		
WBC, pre-vacc. NORMAL (N=184;83), Month 12 BELOW	22	16		
WBC, pre-vacc. NORMAL (N=184;83), Month 12 ABOVE	6	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Tanzanian subjects with clinically relevant abnormalities in parameters assessed

End point title	Number of Tanzanian subjects with clinically relevant abnormalities in parameters assessed

End point description:

Biochemical and haematological parameters assessed were:
Alanine amino-transferase (ALT), basophils (BAS), creatinine (CREA), eosinophils (EOS), hematocrit (HC), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), platelets (PLA), red blood cells (RBC), white blood cells (WBC).
Number of subjects were separated with respect to their results at pre-vaccination, i.e. whether their results were in, above or below the normal range.
N for each category at pre-vaccination noted in category title. For each parameter and for each range it was assessed whether the values of the subjects were in, above or below the normal range.

End point type	Secondary

End point timeframe:

At Month 12

End point values	Cervarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	194	100		
Units: Subjects				
ALT, pre-vacc. ABOVE (N=3;4), Month 12 NORMAL	2	2		
ALT, pre-vacc. ABOVE (N=3;4), Month 12 BELOW	0	1		
ALT, pre-vacc. ABOVE (N=3;4), Month 12 ABOVE	1	1		
ALT, pre-vacc. BELOW (N=13;11), Month 12 NORMAL	12	8		
ALT, pre-vacc. BELOW (N=13;11), Month 12 BELOW	1	3		
ALT, pre-vacc. BELOW (N=13;11), Month 12 ABOVE	0	0		
ALT, pre-vacc. NORMAL (N=190;87), Month 12 NORMAL	166	73		
ALT, pre-vacc. NORMAL (N=190;87), Month 12 BELOW	24	13		
ALT, pre-vacc. NORMAL (N=190;87), Month 12 ABOVE	0	1		

BAS, pre-vacc. ABOVE (N=23;13), Month 12 NORMAL	21	12		
BAS, pre-vacc. ABOVE (N=23;13), Month 12 BELOW	0	0		
BAS, pre-vacc. ABOVE (N=23;13), Month 12 ABOVE	2	1		
BAS, pre-vacc. NORMAL (N=183;89), Month 12 NORMAL	174	81		
BAS, pre-vacc. NORMAL (N=183;89), Month 12 BELOW	0	0		
BAS, pre-vacc. NORMAL (N=183;89), Month 12 ABOVE	9	8		
CREA, pre-vacc. BELOW (N=42;14), Month 12 NORMAL	2	0		
CREA, pre-vacc. BELOW (N=42;14), Month 12 BELOW	40	14		
CREA, pre-vacc. BELOW (N=42;14), Month 12 ABOVE	0	0		
CREA, pre-vacc. NORMAL (N=164;88), Month 12 NORMAL	48	19		
CREA, pre-vacc. NORMAL (N=164;88), Month 12 BELOW	116	69		
CREA, pre-vacc. NORMAL (N=164;88), Month 12 ABOVE	0	0		
EOS, pre-vacc. ABOVE (N=79;43), Month 12 NORMAL	22	10		
EOS, pre-vacc. ABOVE (N=79;43), Month 12 BELOW	0	0		
EOS, pre-vacc. ABOVE (N=79;43), Month 12 ABOVE	57	33		
EOS, pre-vacc. NORMAL (N=127;59), Month 12 NORMAL	93	48		
EOS, pre-vacc. NORMAL (N=127;59), Month 12 BELOW	0	0		
EOS, pre-vacc. NORMAL (N=127;59), Month 12 ABOVE	34	11		
HC, pre-vacc. BELOW (N=63;38), Month 12 NORMAL	29	10		
HC, pre-vacc. BELOW (N=63;38), Month 12 BELOW	34	28		
HC, pre-vacc. BELOW (N=63;38), Month 12 ABOVE	0	0		
HC, pre-vacc. NORMAL (N=143;64), Month 12 NORMAL	107	48		
HC, pre-vacc. NORMAL (N=143;64), Month 12 BELOW	36	16		
HC, pre-vacc. NORMAL (N=143;64), Month 12 ABOVE	0	0		
LYM, pre-vacc. ABOVE (N=18;8), Month 12 NORMAL	9	3		
LYM, pre-vacc. ABOVE (N=18;8), Month 12 BELOW	0	0		
LYM, pre-vacc. ABOVE (N=18;8), Month 12 ABOVE	9	5		
LYM, pre-vacc. NORMAL (N=188;94), Month 12 NORMAL	168	81		
LYM, pre-vacc. NORMAL (N=188;94), Month 12 BELOW	0	2		
LYM, pre-vacc. NORMAL (N=188;94), Month 12 ABOVE	20	11		
MON, pre-vacc. ABOVE (N=12;7), Month 12 NORMAL	8	6		

MON, pre-vacc. ABOVE (N=12;7), Month 12 BELOW	0	0		
MON, pre-vacc. ABOVE (N=12;7), Month 12 ABOVE	4	1		
MON, pre-vacc. NORMAL (N=194;95), Month 12 NORMAL	184	88		
MON, pre-vacc. NORMAL (N=194;95), Month 12 BELOW	0	0		
MON, pre-vacc. NORMAL (N=194;95), Month 12 ABOVE	10	7		
NEU, pre-vacc. BELOW (N=36;17), Month 12 NORMAL	18	6		
NEU, pre-vacc. BELOW (N=36;17), Month 12 BELOW	18	11		
NEU, pre-vacc. BELOW (N=36;17), Month 12 ABOVE	0	0		
NEU, pre-vacc. NORMAL (N=170;85), Month 12 NORMAL	138	72		
NEU, pre-vacc. NORMAL (N=170;85), Month 12 BELOW	32	13		
NEU, pre-vacc. NORMAL (N=170;85), Month 12 ABOVE	0	0		
PLA, pre-vacc. ABOVE (N=10;2), Month 12 NORMAL	8	1		
PLA, pre-vacc. ABOVE (N=10;2), Month 12 BELOW	0	0		
PLA, pre-vacc. ABOVE (N=10;2), Month 12 ABOVE	2	1		
PLA, pre-vacc. BELOW (N=5;0), Month 12 NORMAL	5	0		
PLA, pre-vacc. BELOW (N=5;0), Month 12 BELOW	0	0		
PLA, pre-vacc. BELOW (N=5;0), Month 12 ABOVE	0	0		
PLA, pre-vacc. NORMAL (N=191;100), Month 12 NORMAL	185	96		
PLA, pre-vacc. NORMAL (N=191;100), Month 12 BELOW	1	2		
PLA, pre-vacc. NORMAL (N=191;100), Month 12 ABOVE	5	2		
RBC, pre-vacc. ABOVE (N=10;7), Month 12 NORMAL	5	3		
RBC, pre-vacc. ABOVE (N=10;7), Month 12 BELOW	0	0		
RBC, pre-vacc. ABOVE (N=10;7), Month 12 ABOVE	5	4		
RBC, pre-vacc. BELOW (N=3;2), Month 12 NORMAL	2	0		
RBC, pre-vacc. BELOW (N=3;2), Month 12 BELOW	1	2		
RBC, pre-vacc. BELOW (N=3;2), Month 12 ABOVE	0	0		
RBC, pre-vacc. NORMAL (N=193;93), Month 12 NORMAL	182	91		
RBC, pre-vacc. NORMAL (N=193;93), Month 12 BELOW	6	2		
RBC, pre-vacc. NORMAL (N=193;93), Month 12 ABOVE	5	0		
WBC, pre-vacc. ABOVE (N=17;6), Month 12 NORMAL	12	5		
WBC, pre-vacc. ABOVE (N=17;6), Month 12 BELOW	0	0		

WBC, pre-vacc. ABOVE (N=17;6), Month 12 ABOVE	5	1		
WBC, pre-vacc. BELOW (N=0;2), Month 12 NORMAL	0	2		
WBC, pre-vacc. BELOW (N=0;2), Month 12 BELOW	0	0		
WBC, pre-vacc. BELOW (N=0;2), Month 12 ABOVE	0	0		
WBC, pre-vacc. NORMAL (N=189;94), Month 12 NORMAL	165	85		
WBC, pre-vacc. NORMAL (N=189;94), Month 12 BELOW	14	5		
WBC, pre-vacc. NORMAL (N=189;94), Month 12 ABOVE	10	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms: within 7 days (Day 0-6) after vaccination; Unsolicited AEs: within 30 days (Day 0-29) after any vaccination; SAEs: during the whole study period (from Day 0 up to Month 12).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Cervarix Group

Reporting group description:

Healthy female subjects who received 3 doses of Cervarix at Months 0, 1 and 6, administered intramuscularly into the deltoid region of the non-dominant arm. For some analyses the group was stratified by age into a 10-14 years of age group and a 15-25 years of age group.

Reporting group title	Placebo Group

Reporting group description:

Healthy female subjects who received 3 doses of placebo at Months 0, 1 and 6, administered intramuscularly into the deltoid region of the non-dominant arm. For some analyses the group was stratified by age into a 10-14 years of age group and a 15-25 years of age group.

Serious adverse events	Cervarix Group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 450 (3.78%)	14 / 226 (6.19%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous complete			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ectopic pregnancy			

subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postpartum haemorrhage			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Neuropathy vitamin b6 deficiency			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Malaria			

subjects affected / exposed	10 / 450 (2.22%)	11 / 226 (4.87%)	
occurrences causally related to treatment / all	0 / 10	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 450 (0.00%)	3 / 226 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amoebiasis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burn infection			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysentery			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic inflammatory disease			

subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyomyositis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis bacterial			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
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	Placebo Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	433 / 450 (96.22%)	216 / 226 (95.58%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	3 / 450 (0.67%)	2 / 226 (0.88%)	
occurrences (all)	3	2	
Orthostatic hypotension			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Phlebitis			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences (all)	1	1	
Chest discomfort			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	5 / 450 (1.11%)	1 / 226 (0.44%)	
occurrences (all)	5	1	
Fatigue			
subjects affected / exposed	111 / 450 (24.67%)	42 / 226 (18.58%)	
occurrences (all)	130	50	
Influenza like illness			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Injection site rash			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	376 / 450 (83.56%)	168 / 226 (74.34%)	
occurrences (all)	779	279	
Pyrexia			
subjects affected / exposed	147 / 450 (32.67%)	71 / 226 (31.42%)	
occurrences (all)	235	110	
Swelling			
subjects affected / exposed	74 / 450 (16.44%)	27 / 226 (11.95%)	
occurrences (all)	86	32	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			

Amenorrhoea			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Dysmenorrhoea			
subjects affected / exposed	23 / 450 (5.11%)	10 / 226 (4.42%)	
occurrences (all)	25	10	
Genital discharge			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Menstruation delayed			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Metrorrhagia			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences (all)	1	1	
Oligomenorrhoea			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Ovarian cyst			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Pelvic pain			
subjects affected / exposed	3 / 450 (0.67%)	0 / 226 (0.00%)	
occurrences (all)	3	0	
Vaginal discharge			
subjects affected / exposed	6 / 450 (1.33%)	4 / 226 (1.77%)	
occurrences (all)	6	4	
Vaginal haemorrhage			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences (all)	1	1	
Vulvovaginal pruritus			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			

Bronchopneumopathy			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	13 / 450 (2.89%)	7 / 226 (3.10%)	
occurrences (all)	13	8	
Dysphonia			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	8 / 450 (1.78%)	6 / 226 (2.65%)	
occurrences (all)	9	6	
Rhinorrhoea			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	2 / 450 (0.44%)	1 / 226 (0.44%)	
occurrences (all)	2	1	
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Burns first degree			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Human bite			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Limb traumatic amputation			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Soft tissue injury			

subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	2 / 450 (0.44%)	1 / 226 (0.44%)	
occurrences (all)	2	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Head discomfort			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	201 / 450 (44.67%)	116 / 226 (51.33%)	
occurrences (all)	298	157	
Sensory disturbance			
subjects affected / exposed	2 / 450 (0.44%)	0 / 226 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Lymphadenitis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	5 / 450 (1.11%)	2 / 226 (0.88%)	
occurrences (all)	5	2	
Vertigo			
subjects affected / exposed	13 / 450 (2.89%)	3 / 226 (1.33%)	
occurrences (all)	15	4	
Eye disorders			

Conjunctivitis			
subjects affected / exposed	8 / 450 (1.78%)	1 / 226 (0.44%)	
occurrences (all)	8	1	
Conjunctivitis allergic			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Eye allergy			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Eye irritation			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Eye pain			
subjects affected / exposed	4 / 450 (0.89%)	0 / 226 (0.00%)	
occurrences (all)	4	0	
Eye pruritus			
subjects affected / exposed	2 / 450 (0.44%)	0 / 226 (0.00%)	
occurrences (all)	2	0	
Eyelid oedema			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences (all)	1	1	
Lacrimation increased			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences (all)	1	1	
Myopia			
subjects affected / exposed	1 / 450 (0.22%)	2 / 226 (0.88%)	
occurrences (all)	1	2	
Visual impairment			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Abdominal pain			

subjects affected / exposed	16 / 450 (3.56%)	7 / 226 (3.10%)	
occurrences (all)	17	7	
Abdominal pain upper			
subjects affected / exposed	1 / 450 (0.22%)	2 / 226 (0.88%)	
occurrences (all)	1	2	
Constipation			
subjects affected / exposed	0 / 450 (0.00%)	2 / 226 (0.88%)	
occurrences (all)	0	2	
Dental caries			
subjects affected / exposed	6 / 450 (1.33%)	2 / 226 (0.88%)	
occurrences (all)	6	2	
Diarrhoea			
subjects affected / exposed	6 / 450 (1.33%)	3 / 226 (1.33%)	
occurrences (all)	6	3	
Dyspepsia			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Enteritis			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	4 / 450 (0.89%)	0 / 226 (0.00%)	
occurrences (all)	4	0	
Gastrointestinal disorder			
subjects affected / exposed	118 / 450 (26.22%)	56 / 226 (24.78%)	
occurrences (all)	143	66	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Gingivitis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Glossitis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids			

subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Hyperchlorhydria			
subjects affected / exposed	2 / 450 (0.44%)	0 / 226 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	2 / 450 (0.44%)	2 / 226 (0.88%)	
occurrences (all)	2	2	
Oesophagitis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Peptic ulcer			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	6 / 450 (1.33%)	3 / 226 (1.33%)	
occurrences (all)	6	3	
Vomiting			
subjects affected / exposed	2 / 450 (0.44%)	0 / 226 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Dermatitis allergic			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Eczema			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Pigmentation disorder			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	

Pruritus			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	71 / 450 (15.78%)	33 / 226 (14.60%)	
occurrences (all)	84	38	
Rash papular			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Skin disorder			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Skin exfoliation			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	68 / 450 (15.11%)	28 / 226 (12.39%)	
occurrences (all)	81	33	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	79 / 450 (17.56%)	36 / 226 (15.93%)	
occurrences (all)	97	41	
Back pain			
subjects affected / exposed	4 / 450 (0.89%)	2 / 226 (0.88%)	
occurrences (all)	4	2	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Myalgia			

subjects affected / exposed	90 / 450 (20.00%)	38 / 226 (16.81%)	
occurrences (all)	113	46	
Neck pain			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	2 / 450 (0.44%)	2 / 226 (0.88%)	
occurrences (all)	2	2	
Torticollis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Abscess			
subjects affected / exposed	2 / 450 (0.44%)	0 / 226 (0.00%)	
occurrences (all)	2	0	
Abscess limb			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences (all)	1	1	
Adenoiditis			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences (all)	1	1	
Amoebiasis			
subjects affected / exposed	1 / 450 (0.22%)	3 / 226 (1.33%)	
occurrences (all)	1	3	
Arthritis bacterial			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Body tinea			
subjects affected / exposed	7 / 450 (1.56%)	3 / 226 (1.33%)	
occurrences (all)	7	3	
Bronchitis			
subjects affected / exposed	4 / 450 (0.89%)	4 / 226 (1.77%)	
occurrences (all)	4	4	
Bronchopneumonia			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	

Candidiasis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Cellulitis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Chlamydial infection			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Cutaneous larva migrans			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	2 / 450 (0.44%)	1 / 226 (0.44%)	
occurrences (all)	2	1	
Fungal skin infection			
subjects affected / exposed	4 / 450 (0.89%)	2 / 226 (0.88%)	
occurrences (all)	4	2	
Gastroenteritis			
subjects affected / exposed	3 / 450 (0.67%)	1 / 226 (0.44%)	
occurrences (all)	3	1	
Giardiasis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Gingival infection			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Helminthic infection			
subjects affected / exposed	8 / 450 (1.78%)	1 / 226 (0.44%)	
occurrences (all)	8	1	
Hookworm infection			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences (all)	1	1	
Hordeolum			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences (all)	1	1	

Influenza			
subjects affected / exposed	8 / 450 (1.78%)	1 / 226 (0.44%)	
occurrences (all)	8	1	
Malaria			
subjects affected / exposed	56 / 450 (12.44%)	38 / 226 (16.81%)	
occurrences (all)	66	44	
Measles			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	9 / 450 (2.00%)	12 / 226 (5.31%)	
occurrences (all)	10	12	
Otitis media			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Parasitic gastroenteritis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Paronychia			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Pelvic inflammatory disease			
subjects affected / exposed	4 / 450 (0.89%)	1 / 226 (0.44%)	
occurrences (all)	5	1	
Pericoronitis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	2 / 450 (0.44%)	0 / 226 (0.00%)	
occurrences (all)	2	0	
Pneumonia			
subjects affected / exposed	2 / 450 (0.44%)	3 / 226 (1.33%)	
occurrences (all)	2	3	
Respiratory tract infection			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences (all)	1	1	

Rhinitis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Sepsis			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Shigella infection			
subjects affected / exposed	0 / 450 (0.00%)	1 / 226 (0.44%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Subcutaneous abscess			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Tinea capitis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Tinea versicolour			
subjects affected / exposed	1 / 450 (0.22%)	1 / 226 (0.44%)	
occurrences (all)	1	1	
Tonsillitis			
subjects affected / exposed	4 / 450 (0.89%)	2 / 226 (0.88%)	
occurrences (all)	4	2	
Trichuriasis			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	10 / 450 (2.22%)	5 / 226 (2.21%)	
occurrences (all)	11	5	
Vaginal infection			
subjects affected / exposed	2 / 450 (0.44%)	0 / 226 (0.00%)	
occurrences (all)	2	0	
Vaginitis bacterial			
subjects affected / exposed	1 / 450 (0.22%)	0 / 226 (0.00%)	
occurrences (all)	1	0	

Varicella subjects affected / exposed occurrences (all)	1 / 450 (0.22%) 1	0 / 226 (0.00%) 0	
Vulvitis subjects affected / exposed occurrences (all)	1 / 450 (0.22%) 1	2 / 226 (0.88%) 2	
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	1 / 450 (0.22%) 1	0 / 226 (0.00%) 0	
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 450 (0.00%) 0	1 / 226 (0.44%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 July 2007	- The global sample size has decreased from 999 subjects to 666 subjects. - The temperature monitoring devices used during storage of the vaccine have been changed. - Cervarix has been licensed in Australia, Kenya and the United Arab Emirates. - An abbreviated title has been added to the Title Page. - Medical history to include information concerning contraception and smoking. The medical history will also be obtained at Visit 1 in addition to the screening visit, and the medical history information is to be recorded in the eCRF.
12 December 2008	- Two interim analyses (1 and 2) have been added which will be performed when: (1) all subjects enrolled in Senegal have completed Visit 6 (Month 7) and (2) all subjects in Tanzania have completed Visit 6 (Month 7). This takes into account different rates of study activities in the two countries and enables the analysis of results from the different countries separately. - The list of study procedures, study design overview and statistical considerations have been updated to include the two interim analyses. - The list of contributing authors has been updated. - Reference to the current version of the IB and recent references have been added. - Minor corrections such as inconsistencies, formatting and typos have been made. - For clarity, cross-referencing to the first amendment has been removed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported