



Clinical trial results:

A phase IIIb, open, multi-country, controlled, randomized study to demonstrate the immunogenicity and safety of GSK Biologicals' meningococcal conjugate vaccine, MenACWY-TT (GSK 134612) in healthy infants, given on a 3+1 primary and booster (2, 4, 6 and 15-18 months of age), a 1+1 primary and booster (6 and 15-18 months of age) or as a single dose at 15-18 months of age

Summary

EudraCT number	2013-002537-37
Trial protocol	Outside EU/EEA
Global end of trial date	

Results information

Result version number	v1
This version publication date	29 April 2016
First version publication date	29 April 2016

Trial information

Trial identification

Sponsor protocol code	114858
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01340898
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, 1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, 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?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	12 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 August 2014
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the immunogenicity of the MenACWY-TT conjugate vaccine in terms of bactericidal antibodies to *N. meningitidis* serogroups A, C, W-135 and Y one month post-dose 3 of MenACWY-TT at 7 months of age in healthy infants.

Criteria for immunogenicity:

For each serogroup, one month after dose 3 of MenACWY-TT vaccination, the lower limit of the two-sided exact 95% confidence interval (CI) for the percentage of subjects with rSBA titre $\geq 1:8$ is greater than or equal to the pre-defined clinical limit of 80%.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 January 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Mexico: 351
Country: Number of subjects enrolled	Lebanon: 402
Worldwide total number of subjects	753
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)	753

Children (2-11 years)	0
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: -

Pre-assignment

Screening details:

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

Period 1

Period 1 title	Primary Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix 3+1 Group

Arm description:

Subjects who received 3 doses of Nimenrix™ vaccine at 3 doses at 2, 4 and 6 months of age.

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	MenACWY-TT vaccine, GSK134612
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The 3 vaccine doses were administered in the anterolateral region of the thigh at 2, 4 and 6 months of age.

Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	10Pn vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

As part of the study all subjects received routine administration of Synflorix at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Infanrix-IPV vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Hib vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

Arm title	Nimenrix 1+1 Group
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Arm description:

Subjects who received 1 dose of Nimenrix vaccine 1 dose at 6 months of age.

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	MenACWY-TT vaccine, GSK134612
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered in the anterolateral region of the thigh at 6 months of age.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Infanrix-IPV vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Hib vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	10Pn vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

As part of the study all subjects received routine administration of Synflorix at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

Arm title	Nimenrix 1 Group
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Arm description:

Subjects who received routine administration of Infanrix-IPV, Hiberix and Synflorix at 2, 4 and 6 months of age.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Infanrix-IPV vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Hib vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	10Ph vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

As part of the study all subjects received routine administration of Synflorix at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

Number of subjects in period 1^[1]	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group
Started	376	187	187
Completed	360	178	181
Not completed	16	9	6
Consent withdrawn by subject	8	7	5
Migrated/moved from study area	4	1	-
Serious adverse event	-	-	1
Lost to follow-up	4	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Not all subjects who completed a period entered in the next one . The number of subjects who started each period depends on the number of subjects available at the time.

Period 2

Period 2 title	Booster Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	Nimenrix 3+1 Group
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Arm description:

Subjects who received 1 dose of Nimenrix™ vaccine at 15-18 months of age.

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	MenACWY-TT vaccine, GSK134612
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered in the anterolateral region of the thigh at 15-18 months of age.

Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	10Pn vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

As part of the study all subjects received routine administration of Synflorix at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Infanrix-IPV vaccine at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Hib vaccine at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

Arm title	Nimenrix 1+1 Group
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Arm description:

Subjects who received 1 dose of Nimenrix vaccine 15-18 months of age.

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	MenACWY-TT vaccine, GSK134612
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered in the anterolateral region of the thigh at 15-18 months of age.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Infanrix-IPV vaccine at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Hib vaccine at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	10Pn vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

As part of the study all subjects received routine administration of Synflorix at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

Arm title	Nimenrix 1 Group
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Arm description:

Subjects who received 1 dose of Nimenrix vaccine at 15-18 months of age.

Arm type	Active comparator
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	MenACWY-TT vaccine, GSK134612
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered in the anterolateral region of the thigh at 15-18 months of age.

Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	10Pn vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

As part of the study all subjects received routine administration of Synflorix at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Hib vaccine at 15-18 months of age,

administered intramuscularly (IM) in the anterolateral region of the thigh.

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

Dosage and administration details:

As part of the study all subjects received routine administration of Infanrix-IPV vaccine at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

Number of subjects in period 2^[2]	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group
Started	342	166	170
Completed	332	164	163
Not completed	10	2	7
Consent withdrawn by subject	3	-	4
Migrated/moved from study area	3	-	-
Lost to follow-up	4	2	3

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all subjects who completed a period entered in the next one . The number of subjects who started each period depends on the number of subjects available at the time.

Baseline characteristics

Reporting groups

Reporting group title	Nimenrix 3+1 Group
Reporting group description:	
Subjects who received 3 doses of Nimenrix™ vaccine at 3 doses at 2, 4 and 6 months of age.	
Reporting group title	Nimenrix 1+1 Group
Reporting group description:	
Subjects who received 1 dose of Nimenrix vaccine 1 dose at 6 months of age.	
Reporting group title	Nimenrix 1 Group
Reporting group description:	
Subjects who received routine administration of Infanrix-IPV, Hiberix and Synflorix at 2, 4 and 6 months of age.	

Reporting group values	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group
Number of subjects	376	187	187
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: months			
arithmetic mean	8.1	8.1	8.2
standard deviation	± 1.6	± 1.7	± 1.7
Gender categorical			
Units: Subjects			
Female	182	105	95
Male	194	82	92

Reporting group values	Total		
Number of subjects	750		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		

Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: months			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	382		
Male	368		

End points

End points reporting groups

Reporting group title	Nimenrix 3+1 Group
Reporting group description: Subjects who received 3 doses of Nimenrix™ vaccine at 3 doses at 2, 4 and 6 months of age.	
Reporting group title	Nimenrix 1+1 Group
Reporting group description: Subjects who received 1 dose of Nimenrix vaccine 1 dose at 6 months of age.	
Reporting group title	Nimenrix 1 Group
Reporting group description: Subjects who received routine administration of Infanrix-IPV, Hiberix and Synflorix at 2, 4 and 6 months of age.	
Reporting group title	Nimenrix 3+1 Group
Reporting group description: Subjects who received 1 dose of Nimenrix™ vaccine at 15-18 months of age.	
Reporting group title	Nimenrix 1+1 Group
Reporting group description: Subjects who received 1 dose of Nimenrix vaccine 15-18 months of age.	
Reporting group title	Nimenrix 1 Group
Reporting group description: Subjects who received 1 dose of Nimenrix vaccine at 15-18 months of age.	

Primary: Number of subjects with meningococcal polysaccharide A serum bactericidal assay using baby rabbit complement (rSBA-MenA) titers $\geq 1:8$

End point title	Number of subjects with meningococcal polysaccharide A serum bactericidal assay using baby rabbit complement (rSBA-MenA) titers $\geq 1:8$ ^[1]
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End point description:

End point type	Primary
End point timeframe: One month following Dose 3	

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: Results will be updated when they become available.

End point values	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[2]	0 ^[3]	0 ^[4]	
Units: Subjects				
rSBA-MenA, D3				

Notes:

[2] - Immunogenicity results will be updated when they become available.

[3] - Immunogenicity results will be updated when they become available.

[4] - Immunogenicity results will be updated when they become available.

Statistical analyses

Secondary: Number of subjects with solicited local symptoms (PRI)

End point title	Number of subjects with solicited local symptoms (PRI)
End point description:	
End point type	Secondary
End point timeframe:	
Withing 8 days (Day 0-7) post primary vaccination	

End point values	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	369	182	184	
Units: Subjects				
Any Pain Dose 1 [N=369;182;184]	220	115	108	
Grade 3 Pain Dose 1 [N=369;182;184]	38	25	14	
Any Redness Dose 1 [N=369;182;184]	94	39	43	
Grade 3 Redness Dose 1 [N=369;182;184]	1	0	0	
Any Swelling Dose 1 [N=369;182;184]	84	31	34	
Grade 3 Swelling Dose 1 [N=369;182;184]	0	3	0	
Any Pain Dose 2 [N=363;181;181]	177	92	101	
Grade 3 Pain Dose 2 [N=363;181;181]	33	11	16	
Any Redness Dose 2 [N=363;181;181]	93	51	48	
Grade 3 Redness Dose 2 [N=363;181;181]	2	0	1	
Any Swelling Dose 2 [N=363;181;181]	76	47	42	
Grade 3 Swelling Dose 2 [N=363;181;181]	2	2	0	
Any Pain Dose 3 [N=359;177;180]	148	73	93	
Grade 3 Pain Dose 3 [N=359;177;180]	16	18	9	
Any Redness Dose 3 [N=359;177;180]	74	46	42	
Grade 3 Redness Dose 3 [N=359;177;180]	1	1	1	
Any Swelling Dose 3 [N=359;177;180]	66	46	37	
Grade 3 Swelling Dose 3 [N=359;177;180]	1	0	0	
Any Pain Across Doses [N=369;182;184]	262	135	142	
Grade 3 Pain Across Doses [N=369;182;184]	65	36	33	
Any Redness Across Doses [N=369;182;184]	160	79	78	
Grade 3 Redness Across Doses [N=369;182;184]	4	1	2	
Any Swelling Across Doses [N=369;182;184]	147	74	70	
Grade 3 Swelling Across Doses [N=369;182;184]	3	4	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms (BST)

End point title	Number of subjects with solicited local symptoms (BST)
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End point description:

End point type	Secondary
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End point timeframe:

Within 8 days (Day 0-7) post booster vaccination

End point values	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	338	165	167	
Units: Subjects				
Any Pain	139	71	77	
Grade 3 Pain	21	19	14	
Any Redness	74	32	39	
Grade 3 Redness	1	1	3	
Any Swelling	55	29	33	
Grade 3 Swelling	2	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms (PRI)

End point title	Number of subjects with solicited general symptoms (PRI)
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End point description:

End point type	Secondary
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End point timeframe:

Within 8 days (Day 0-7) post primary vaccination

End point values	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	369	182	184	
Units: Subjects				
Any Drowsiness Dose 1 [N=369;182;184]	177	93	84	
Grade 3 Drowsiness Dose 1 [N=369;182;184]	18	10	2	
Related Drowsiness Dose 1 [N=369;182;184]	160	84	79	
Any Irritability Dose 1 [N=369;182;184]	200	107	99	
Grade 3 Irritability Dose 1 [N=369;182;184]	19	9	10	
Related Irritability Dose 1 [N=369;182;184]	188	96	89	
Any Loss of appetite Dose 1 [N=369;182;184]	109	62	42	
Grade 3 Loss of appetite Dose 1 [N=369;182;184]	7	5	3	
Related Loss of appetite Dose 1 [N=369;182;184]	99	55	35	
Any Temperature Dose 1 [N=369;182;184]	126	62	58	
Grade 3 Temperature Dose 1 [N=369;182;184]	0	0	1	
Related Temperature Dose 1 [N=369;182;184]	109	56	53	
Any Drowsiness Dose 2 [N=363;181;181]	116	72	67	
Grade 3 Drowsiness Dose 2 [N=363;181;181]	9	8	8	
Related Drowsiness Dose 2 [N=363;181;181]	109	69	62	
Any Irritability Dose 2 [N=363;181;181]	163	82	90	
Grade 3 Irritability Dose 2 [N=363;181;181]	20	14	10	
Related Irritability Dose 2 [N=363;181;181]	158	77	85	
Any Loss of appetite Dose 2 [N=363;181;181]	89	50	44	
Grade 3 Loss of appetite Dose 2 [N=363;181;181]	6	5	6	
Related Loss of appetite Dose 2 [N=363;181;181]	80	48	39	
Any Temperature Dose 2 [N=363;181;181]	119	64	63	
Grade 3 Temperature Dose 2 [N=363;181;181]	0	0	0	
Related Temperature Dose 2 [N=363;181;181]	116	59	54	
Any Drowsiness Dose 3 [N=359;177;180]	102	54	64	
Grade 3 Drowsiness Dose 3 [N=359;177;180]	11	8	4	
Related Drowsiness Dose 3 [N=359;177;180]	95	54	60	
Any Irritability Dose 3 [N=359;177;180]	140	73	73	
Grade 3 Irritability Dose 3 [N=359;177;180]	14	14	3	

Related Irritability Dose 3 [N=359;177;180]	132	72	69	
Any Loss of appetite Dose 3 [N=359;177;180]	76	43	50	
Grade 3 Loss of appetite Dose 3 [N=359;177;180]	7	6	3	
Related Loss of appetite Dose 3 [N=359;177;180]	63	41	46	
Any Temperature Dose 3 [N=359;177;180]	109	51	41	
Grade 3 Temperature Dose 3 [N=359;177;180]	2	0	0	
Related Temperature Dose 3 [N=359;177;180]	96	46	36	
Any Drowsiness Across Doses [N=369;182;184]	217	121	118	
Grade 3 Drowsiness Across Doses [N=369;182;184]	30	19	13	
Related Drowsiness Across Doses [N=369;182;184]	205	116	114	
Any Irritability Across Doses [N=369;182;184]	254	128	126	
Grade 3 Irritability Across Doses [N=369;182;184]	42	27	18	
Related Irritability Across Doses [N=369;182;184]	246	125	121	
Any Loss of appetite Across [N=369;182;184]	165	89	82	
Grade 3 Loss of appetite Across [N=369;182;184]	17	13	10	
Related Loss of appetite Across [N=369;182;184]	151	84	77	
Any Temperature Across Doses [N=369;182;184]	203	102	101	
Grade 3 Temperature Across Doses [N=369;182;184]	2	0	1	
Related Temperature Across Doses [N=369;182;184]	193	97	93	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms (BST)

End point title	Number of subjects with solicited general symptoms (BST)
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End point description:

End point type	Secondary
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End point timeframe:

Within 8 days (Day 0-7) post booster vaccination

End point values	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	338	165	167	
Units: Subjects				
Any Drowsiness	79	46	43	
Grade 3 Drowsiness	4	7	5	
Related Drowsiness	75	42	43	
Any Irritability	112	54	61	
Grade 3 Irritability	9	12	10	
Related Irritability	106	52	60	
Any Loss of appetite	69	37	39	
Grade 3 Loss of appetite	5	5	1	
Related Loss of appetite	60	34	37	
Any Temperature	68	35	27	
Grade 3 Temperature	2	1	0	
Related Temperature	62	32	24	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs) (PRI)

End point title	Number of subjects with unsolicited adverse events (AEs) (PRI)
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End point description:

End point type	Secondary
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End point timeframe:

Withing 31 days (Day 0-30) post each primary vaccine dose

End point values	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	376	187	187	
Units: Subjects				
Any AE(s) Dose 1 [N=376;187;187]	67	36	34	
Any AE(s) Dose 2 [N=368;182;182]	70	34	28	
Any AE(s) Dose 3 [N=362;179;181]	97	49	45	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs) (BST)

End point title	Number of subjects with unsolicited adverse events (AEs) (BST)
End point description:	
End point type	Secondary
End point timeframe:	
Within 31 days (Day 0-30) post booster vaccination	

End point values	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	342	166	170	
Units: Subjects				
Any AE(s)	58	32	36	

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:	
End point type	Secondary
End point timeframe:	
During the entire study period	

End point values	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	376	187	187	
Units: Subjects				
Any SAE(s)	35	14	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with new onset of chronic illnesses (NOCIs)

End point title	Number of subjects with new onset of chronic illnesses (NOCIs)
End point description:	

End point type	Secondary
End point timeframe:	
During the entire study period	

End point values	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	376	187	187	
Units: Subjects				
Any NOCI(s)	16	8	4	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: within 8 days (Day 0-Day 7), AEs: within 31 days (Day 0 – Day 30), SAEs: throughout the study period.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	Nimenrix 3+1 Group
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Reporting group description:

Subjects who receive 3 primary doses of the investigational vaccine at 2, 4 and 6 months of age and 1 booster dose at 15-18 months of age

Reporting group title	Nimenrix 1+1 Group
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Reporting group description:

Subjects received 1 primary vaccination dose of the investigational vaccine at 6 months of age and 1 booster dose at 15-18 months of age

Reporting group title	Nimenrix 1 Group
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Reporting group description:

Subjects received 1 dose of the investigational vaccine at 15-18 months of age

Serious adverse events	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 376 (9.31%)	14 / 187 (7.49%)	14 / 187 (7.49%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 376 (0.00%)	2 / 187 (1.07%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burns first degree			
subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burns second degree			

subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body			
subjects affected / exposed	0 / 376 (0.00%)	0 / 187 (0.00%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	0 / 376 (0.00%)	1 / 187 (0.53%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 376 (0.00%)	1 / 187 (0.53%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 376 (0.00%)	0 / 187 (0.00%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 376 (0.27%)	1 / 187 (0.53%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 376 (0.00%)	1 / 187 (0.53%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemic seizure			

subjects affected / exposed	0 / 376 (0.00%)	0 / 187 (0.00%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 376 (0.53%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden infant death syndrome			
subjects affected / exposed	0 / 376 (0.00%)	0 / 187 (0.00%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 376 (0.27%)	1 / 187 (0.53%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic shock			
subjects affected / exposed	0 / 376 (0.00%)	1 / 187 (0.53%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Milk allergy			
subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 376 (0.53%)	0 / 187 (0.00%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus paralytic			

subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Lung disorder			
subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	13 / 376 (3.46%)	2 / 187 (1.07%)	3 / 187 (1.60%)
occurrences causally related to treatment / all	0 / 16	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	5 / 376 (1.33%)	1 / 187 (0.53%)	3 / 187 (1.60%)
occurrences causally related to treatment / all	0 / 7	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	4 / 376 (1.06%)	1 / 187 (0.53%)	3 / 187 (1.60%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	3 / 376 (0.80%)	0 / 187 (0.00%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 376 (0.53%)	2 / 187 (1.07%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 376 (0.27%)	2 / 187 (1.07%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastroenteritis viral			
subjects affected / exposed	2 / 376 (0.53%)	0 / 187 (0.00%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	0 / 376 (0.00%)	0 / 187 (0.00%)	2 / 187 (1.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	1 / 376 (0.27%)	1 / 187 (0.53%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	1 / 376 (0.27%)	1 / 187 (0.53%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amoebic dysentery			
subjects affected / exposed	0 / 376 (0.00%)	1 / 187 (0.53%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctivitis			
subjects affected / exposed	0 / 376 (0.00%)	0 / 187 (0.00%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	0 / 376 (0.00%)	0 / 187 (0.00%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Measles			

subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurological infection			
subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 376 (0.00%)	1 / 187 (0.53%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Roseola			
subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 376 (0.00%)	1 / 187 (0.53%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 376 (0.27%)	0 / 187 (0.00%)	0 / 187 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 376 (0.53%)	1 / 187 (0.53%)	1 / 187 (0.53%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Nimenrix 3+1 Group	Nimenrix 1+1 Group	Nimenrix 1 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	262 / 376 (69.68%)	135 / 187 (72.19%)	142 / 187 (75.94%)
General disorders and administration site conditions			
Pain (Primary)			
subjects affected / exposed ^[1]	262 / 369 (71.00%)	135 / 182 (74.18%)	142 / 184 (77.17%)
occurrences (all)	262	135	142
Redness (Primary)			
subjects affected / exposed ^[2]	160 / 369 (43.36%)	79 / 182 (43.41%)	78 / 184 (42.39%)
occurrences (all)	160	79	78
Swelling (Primary)			
subjects affected / exposed ^[3]	147 / 369 (39.84%)	74 / 182 (40.66%)	70 / 184 (38.04%)
occurrences (all)	147	74	70
Pain (Booster)			
subjects affected / exposed ^[4]	139 / 338 (41.12%)	71 / 165 (43.03%)	77 / 167 (46.11%)
occurrences (all)	139	71	77
Redness (Booster)			
subjects affected / exposed ^[5]	74 / 338 (21.89%)	32 / 165 (19.39%)	39 / 167 (23.35%)
occurrences (all)	74	32	39
Swelling (Booster)			
subjects affected / exposed ^[6]	55 / 338 (16.27%)	29 / 165 (17.58%)	33 / 167 (19.76%)
occurrences (all)	55	29	33
Drowsiness (Primary)			
subjects affected / exposed ^[7]	217 / 369 (58.81%)	121 / 182 (66.48%)	118 / 184 (64.13%)
occurrences (all)	217	121	118
Irritability (Primary)			
subjects affected / exposed ^[8]	254 / 369 (68.83%)	128 / 182 (70.33%)	126 / 184 (68.48%)
occurrences (all)	254	128	126
Loss of appetite (Primary)			
subjects affected / exposed ^[9]	165 / 369 (44.72%)	89 / 182 (48.90%)	82 / 184 (44.57%)
occurrences (all)	165	89	82
Temperature(Rectally) (Primary)			

subjects affected / exposed ^[10]	203 / 369 (55.01%)	102 / 182 (56.04%)	101 / 184 (54.89%)
occurrences (all)	203	102	101
Drowsiness (Booster)			
subjects affected / exposed ^[11]	79 / 338 (23.37%)	46 / 165 (27.88%)	43 / 167 (25.75%)
occurrences (all)	79	46	43
Irritability (Booster)			
subjects affected / exposed ^[12]	112 / 338 (33.14%)	54 / 165 (32.73%)	61 / 167 (36.53%)
occurrences (all)	112	54	61
Loss of appetite (Booster)			
subjects affected / exposed ^[13]	69 / 338 (20.41%)	37 / 165 (22.42%)	39 / 167 (23.35%)
occurrences (all)	69	37	39
Temperature(Rectally) (Booster)			
subjects affected / exposed ^[14]	68 / 338 (20.12%)	35 / 165 (21.21%)	27 / 167 (16.17%)
occurrences (all)	68	35	27
Infections and infestations			
Nasopharyngitis (Booster)			
subjects affected / exposed ^[15]	17 / 342 (4.97%)	12 / 166 (7.23%)	7 / 170 (4.12%)
occurrences (all)	17	12	7
Nasopharyngitis (Primary)			
subjects affected / exposed ^[16]	31 / 362 (8.56%)	14 / 179 (7.82%)	10 / 181 (5.52%)
occurrences (all)	31	14	10
Pharyngitis			
subjects affected / exposed ^[17]	17 / 362 (4.70%)	13 / 179 (7.26%)	12 / 181 (6.63%)
occurrences (all)	17	13	12

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[16] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[17] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 July 2011	Amendment 1 One of the participating countries has requested that the subjects enrolled in that country be vaccinated with acellualr pertussis vaccine instead of whole cell pertussis vaccine in order to align with the national recommendation. On account of this request the following changes have been made in the protocol as part of this amendment. • All subjects will be co-administrated with Infanrix-IPV/Hiberix instead of Tritanrix-HepB/Hiberix that was foreseen in the original protocol. Consequently, changes have been made in the exclusion and elimination criteria, assays, secondary endpoints and the statistical analysis section. - HepB, and whole cell pertussis assays have been removed and assays for the evaluation of acellular pertussis and polio type 1, 2 and 3 have been included. - Secondary endpoints and the statistical analysis sections have been modified to remove whole cell pertussis and HepB analysis and to include acellular pertussis and polio type 1, 2 and 3 analysis. - Exclusion and elimination criteria have been revised based on the change in the co-administered vaccines • Subjects will receive both primary and booster doses of Infanrix-IPV/Hiberix • Interval during which concomitant vaccinations are allowed has been clarified in the exclusion and elimination criteria to ensure that no concomitant vaccination is given during the period between a study vaccine administration and the subsequent blood sampling visit, if applicable.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported