Clinical trial results:
A phase III, randomized, open, controlled, multicenter primary vaccination study to demonstrate the non inferiority of the immunogenicity of GSK Biologicals' meningococcal serogroup ACWY conjugate vaccine when given as one dose with Twinrix™ versus GSK Biologicals' meningococcal serogroup ACWY conjugate vaccine alone and versus Twinrix™ alone in healthy subjects aged 11 through 17 years

Summary

EudraCT number	2006-005999-41
Trial protocol	SE DK
Global end of trial date	28 April 2008

Results information

Result version number	v1
This version publication date	11 May 2016
First version publication date	26 February 2015

Trial information

Trial identification

Sponsor protocol code	109063

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00465816
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium,
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 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	23 January 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 April 2008
Global end of trial reached?	Yes
Global end of trial date	28 April 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of the MenACWY-TT conjugate vaccine co-administered with Twinrix as compared to the MenACWY-TT conjugate vaccine administered alone with respect to the serum bactericidal antibody geometric mean titres as measured using baby rabbit complement (rSBA GMTs) for N. meningitidis serogroups A, C, W-135 and Y.
To demonstrate the non-inferiority of the MenACWY-TT conjugate vaccine co-administered with Twinrix as compared to Twinrix administered alone with respect to the percentage of seroconversion for hepatitis A and percentage of seroprotection for hepatitis B.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 April 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 337
Country: Number of subjects enrolled	Denmark: 274
Worldwide total number of subjects	611
EEA total number of subjects	611

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)	0
Adolescents (12-17 years)	611
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 was performed: informed consent was obtained and signed from parents or guardians of subjects, check for inclusion/exclusion criteria and contraindications/precautions was performed, and medical history of subjects was collected.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix + Twinrix Group

Arm description:

Subjects received 1 dose of Nimenrix™ vaccine at Month 0 and 1 dose of Twinrix™ vaccine at Months 0, 1 and 6.

Arm type	Experimental
Investigational medicinal product name	Nimenrix (Meningococcal vaccine 134612)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose intramuscular injection

Investigational medicinal product name	Twinrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection.
Twinrix Adult will be administered to subjects aged 16 years and above and Twinrix Junior will be administered to subjects aged from 11 years up to and including 15 years of age.

Arm title	Nimenrix Group

Arm description:

Subjects received 1 dose of Nimenrix™ vaccine at Month 0.

Arm type	Active comparator
Investigational medicinal product name	Nimenrix (Meningococcal vaccine 134612)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose intramuscular injection

Arm title	Twinrix Group

Arm description:

Subjects received 1 dose of Twinrix™ vaccine at Months 0, 1 and 6.

Arm type	Active comparator
Investigational medicinal product name	Twinrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection.
Twinrix Adult will be administered to subjects aged 16 years and above and Twinrix Junior will be administered to subjects aged from 11 years up to and including 15 years of age.

Number of subjects in period 1	Nimenrix + Twinrix Group	Nimenrix Group	Twinrix Group
Started	367	122	122
Completed	367	122	120
Not completed	0	0	2
Lost to follow-up	-	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Nimenrix + Twinrix Group
Reporting group description:	
Subjects received 1 dose of Nimenrix™ vaccine at Month 0 and 1 dose of Twinrix™ vaccine at Months 0, 1 and 6.	
Reporting group title	Nimenrix Group
Reporting group description:	
Subjects received 1 dose of Nimenrix™ vaccine at Month 0.	
Reporting group title	Twinrix Group
Reporting group description:	
Subjects received 1 dose of Twinrix™ vaccine at Months 0, 1 and 6.	

Reporting group values	Nimenrix + Twinrix Group	Nimenrix Group	Twinrix Group
Number of subjects	367	122	122
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: years			
log mean	14.3	14.3	14.3
standard deviation	± 1.89	± 1.84	± 1.94
Gender categorical Units: Subjects			
Female	195	61	68
Male	172	61	54

Reporting group values	Total		
Number of subjects	611		
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: years			
log mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	324		
Male	287		

End points

End points reporting groups

Reporting group title	Nimenrix + Twinrix Group
Reporting group description:	
Subjects received 1 dose of Nimenrix™ vaccine at Month 0 and 1 dose of Twinrix™ vaccine at Months 0, 1 and 6.	
Reporting group title	Nimenrix Group
Reporting group description:	
Subjects received 1 dose of Nimenrix™ vaccine at Month 0.	
Reporting group title	Twinrix Group
Reporting group description:	
Subjects received 1 dose of Twinrix™ vaccine at Months 0, 1 and 6.	

Primary: Antibody titers for meningococcal polysaccharide serum bactericidal assay using baby rabbit complement (rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY)

End point title	Antibody titers for meningococcal polysaccharide serum bactericidal assay using baby rabbit complement (rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY)[1]
End point description:	
At 1 month after vaccination with Nimenrix vaccine (Month 1)	
End point type	Primary
End point timeframe:	
At 1 month after vaccination with Nimenrix vaccine (Month 1)	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	360	115		
Units: Titer				
geometric mean (confidence interval 95%)				
rSBA-MenA (N= 353; 113)	5263.9 (4818 to 5751)	5211.7 (4509.8 to 6022.8)		
rSBA-MenC (N= 360; 115)	4344.6 (3800.3 to 4966.8)	4926.9 (3684.8 to 6587.7)		
rSBA-MenW-135 (N= 360; 115)	8922.1 (8278.4 to 9615.9)	8987.7 (7628.9 to 10588.6)		
rSBA-MenY (N= 360; 115)	9291.5 (8537.7 to 10111.9)	9492.8 (8172.4 to 11026.6)		

Statistical analyses

Statistical analysis title	Non-inferiority in term of rSBA-MenA GMT

Statistical analysis description:

To assess the Non-inferiority of the Nimenrix + Twinrix group compared to Nimenrix one, Two-sided 95% CI from ANCOVA model on the GMTs ratio (Nimenrix+Twinrix group over Nimenrix group) was computed. The model was adjusted for age strata and baseline titre. Non-inferiority criterion: Lower limit of the two-sided 95% CI ≥ 0.5.

Comparison groups	Nimenrix + Twinrix Group v Nimenrix Group
Number of subjects included in analysis	475
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Adjusted GMT ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.22

Statistical analysis title	Non-inferiority in term of rSBA-MenC GMT

Statistical analysis description:

To assess the Non-inferiority of the Nimenrix+Twinrix group compared to Nimenrix one, Two-sided 95% CI from ANCOVA model on the GMTs ratio (Nimenrix+Twinrix group over Nimenrix group) was computed. The model was adjusted for age strata and baseline titre.

Non-inferiority criterion: Lower limit of the two-sided 95% CI ≥ 0.5.

Comparison groups	Nimenrix + Twinrix Group v Nimenrix Group
Number of subjects included in analysis	475
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Adjusted GMT ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.21

Statistical analysis title	Non-inferiority in term of rSBA-MenW-135 GMT

Statistical analysis description:

To assess the Non-inferiority of the Nimenrix+Twinrixgroup compared to Nimenrix one, Two-sided 95% CI from ANCOVA model on the GMTs ratio (Nimenrix+Twinrix group over Nimenrix group) was computed. The model was adjusted for age strata and baseline titre.

Non-inferiority criterion: Lower limit of the two-sided 95% CI ≥ 0.5.

Comparison groups	Nimenrix Group v Nimenrix + Twinrix Group

Number of subjects included in analysis	475
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Adjusted GMT ratio
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.19

Statistical analysis title	Non-inferiority in term of rSBA-MenY GMT

Statistical analysis description:

To assess the Non-inferiority of the Nimenrix+Twinrixgroup compared to Nimenrix one, Two-sided 95% CI from ANCOVA model on the GMTs ratio (Nimenrix+Twinrix group over Nimenrix group) was computed. The model was adjusted for age strata and baseline titre.

Non-inferiority criterion: Lower limit of the two-sided 95% CI ≥ 0.5.

Comparison groups	Nimenrix + Twinrix Group v Nimenrix Group
Number of subjects included in analysis	475
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Adjusted GMT ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.19

Primary: Number of subjects seroconverted for hepatitis A

End point title	Number of subjects seroconverted for hepatitis A[2]

End point description:

A seroconverted subject was defined as a subject with anti-Hepatitis A virus (HAV) antibody concentration greater than or equal to 15 milli-International Units per Milliliter (mIU/mL) in previously seronegative subjects.

End point type	Primary

End point timeframe:

At 1 month after the third dose of Twinrix vaccine (Month 7)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received hepatitis vaccination (Twinrix).

End point values	Nimenrix + Twinrix Group	Twinrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	321	95		
Units: Subjects				
Subjects	321	95		

Statistical analyses

Statistical analysis title	Non-inferiority in term of seroconversion rate
Comparison groups	Nimenrix + Twinrix Group v Twinrix Group
Number of subjects included in analysis	416
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Percentage difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.19
upper limit	3.9

Notes:

[3] - To assess the Non-inferiority of the Nimenrix+Twinrix group compared to Twinrix one, two-sided standardized asymptotic 95% CI for the difference in seroconversion rates (Nimenrix+Twinrix group minus Twinrix group) was computed.

Non-inferiority criterion: Lower limit of the two-sided standardized asymptotic 95% CI ≥ -10%

Primary: Number of subjects seroprotected for hepatitis B

End point title	Number of subjects seroprotected for hepatitis B[4]

End point description:

A seroprotected subject was defined as a subject with anti-Hepatitis B surface antigen (HBs) antibody concentration greater than or equal to 10 milli-International Units per Milliliter (mIU/mL).

End point type	Primary

End point timeframe:

At 1 month after the third dose of Twinrix vaccine (Month 7)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received hepatitis vaccination (Twinrix).

End point values	Nimenrix + Twinrix Group	Twinrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	97		
Units: Subjects				
Subjects	327	97		

Statistical analyses

Statistical analysis title	Non-inferiority in term of seroprotection rate
Comparison groups	Twinrix Group v Nimenrix + Twinrix Group
Number of subjects included in analysis	427
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Percentage difference
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.64
upper limit	2.92

Notes:

[5] - To assess the Non-inferiority of the Nimenrix+Twinrix group compared to the Twinrix one, two-sided standardized asymptotic 95% CI for the difference in seroprotection rates (Nimenrix+Twinrix group minus Twinrix group) was computed.

Non-inferiority criterion: Lower limit of the two-sided standardized asymptotic 95% CI ≥ -10%

Secondary: Number of subjects with a vaccine response to MenA, MenC, MenY and MenW-135

End point title	Number of subjects with a vaccine response to MenA, MenC, MenY and MenW-135[6]

End point description:

Vaccine response is defined as an rSBA titer of at least 1:32 in subjects initially seronegative [rSBA titer below1:8] and as a 4-fold increase in titer in subjects initially seropositive [rSBA titre greater than or equal to 1:8].

End point type	Secondary

End point timeframe:

At 1 month after vaccination with Nimenrix vaccine (Month 1)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	355	114		
Units: Subjects				
rSBA-MenA (N= 261; 84)	246	76		
rSBA-MenC (N= 355; 112)	333	101		
rSBA-MenW-135 (N= 349; 114)	346	112		
rSBA-MenY (N= 354; 113)	335	105		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and

rSBA-MenY titers above predefined cut-off values

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers above predefined cut-off values[7]

End point description:

The cut-off values assessed were greater than or equal to (≥) 1:8 and ≥ 1:128.

End point type	Secondary

End point timeframe:

Prior to and 1 month after vaccination with Nimenrix vaccine (Months 0 and 1)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	360	115		
Units: Subjects				
rSBA-MenA ≥ 1:8 [Month 0] (N= 266; 85)	105	33		
rSBA-MenA ≥ 1:8 [Month 1] (N= 353; 113)	352	113		
rSBA-MenC ≥ 1:8 [Month 0] (N= 355; 112)	187	67		
rSBA-MenC ≥ 1:8 [Month 1] (N= 360; 115)	359	114		
rSBA-MenW-135 ≥ 1:8 [Month 0] (N= 349; 114)	277	96		
rSBA-MenW-135 ≥ 1:8 [Month 1] (N= 360; 115)	360	115		
rSBA-MenY ≥ 1:8 [Month 0] (N= 354; 113)	275	95		
rSBA-MenY ≥ 1:8 [Month 1] (N= 360; 115)	359	115		
rSBA-MenA ≥ 1:128 [Month 0] (N= 266; 85)	91	30		
rSBA-MenA ≥ 1:128 [Month 1] (N= 353; 113)	352	113		
rSBA-MenC ≥ 1:128 [Month 0] (N= 355; 112)	122	44		
rSBA-MenC ≥ 1:128 [Month 1] (N= 360; 115)	358	113		
rSBA-MenW-135 ≥ 1:128 [Month 0] (N= 349; 114)	180	64		
rSBA-MenW-135 ≥ 1:128 [Month 1] (N= 360; 115)	359	115		
rSBA-MenY ≥ 1:128 [Month 0] (N= 354; 113)	218	80		
rSBA-MenY ≥ 1:128 [Month 1] (N= 360; 115)	359	115		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PSA (polysaccharide A), anti-PSC (polysaccharide C), anti-PSW-135 (polysaccharide W-135), and anti-PSY (polysaccharide Y) antibody concentrations

End point title	Anti-PSA (polysaccharide A), anti-PSC (polysaccharide C), anti-PSW-135 (polysaccharide W-135), and anti-PSY (polysaccharide Y) antibody concentrations[8]

End point description:

Concentrations were provided as Geometric Mean Concentrations expressed as micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

Prior to and 1 month after vaccination with Nimenrix vaccine (Months 0 and 1)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	58		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA [Month 0] (N= 176; 55)	0.25 (0.21 to 0.3)	0.24 (0.19 to 0.31)		
Anti-PSA [Month 1] (N= 179; 56)	27.23 (22.19 to 32.38)	18.47 (12.02 to 28.38)		
Anti-PSC [Month 0] (N= 176; 55)	0.22 (0.19 to 0.26)	0.26 (0.19 to 0.35)		
Anti-PSC [Month 1] (N= 180; 55)	18.58 (15.44 to 22.37)	21.15 (14.87 to 30.09)		
Anti-PSW-135 [Month 0] (N= 176; 58)	0.19 (0.17 to 0.21)	0.16 (0.15 to 0.17)		
Anti-PSW-135 [Month 1] (N= 178; 58)	6.78 (5.52 to 8.32)	6.72 (4.62 to 9.76)		
Anti-PSY [Month 0] (N= 175; 58)	0.22 (0.18 to 0.25)	0.17 (0.14 to 0.21)		
Anti-PSY [Month 1] (N= 180; 55)	14.04 (11.52 to 17.1)	12.5 (8.49 to 18.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-PSA, anti-PSC, anti-PSW-135, and anti-PSY antibody concentrations above pre-defined cut-off values

End point title	Number of subjects with Anti-PSA, anti-PSC, anti-PSW-135, and anti-PSY antibody concentrations above pre-defined cut-off values[9]

End point description:

The cut-off values assessed include greater than or equal to (≥) 0.3 micrograms per milliliter (µg/mL) and ≥ 2.0 µg/mL.

End point type	Secondary

End point timeframe:

Prior to and 1 month after vaccination with Nimenrix vaccine (Months 0 and 1)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	58		
Units: Subjects				
Anti-PSA ≥ 0.3 µg/mL [Month 0] (N= 176; 55)	45	13		
Anti-PSA ≥ 0.3 µg/mL [Month 1] (N= 179; 56)	179	54		
Anti-PSC ≥ 0.3 µg/mL [Month 0] (N= 176; 55)	32	13		
Anti-PSC ≥ 0.3 µg/mL [Month 1] (N= 180; 55)	179	43		
Anti-PSW-135 ≥ 0.3 µg/mL [Month 0] (N= 176; 58)	19	2		
Anti-PSW-135 ≥ 0.3 µg/mL [Month 1] (N= 178; 58)	176	56		
Anti-PSY ≥ 0.3 µg/mL [Month 0] (N= 175; 58)	24	2		
Anti-PSY ≥ 0.3 µg/mL [Month 1] (N= 180; 55)	178	54		
Anti-PSA ≥ 2.0 µg/mL [Month 0] (N= 176; 55)	14	3		
Anti-PSA ≥ 2.0 µg/mL [Month 1] (N= 179; 56)	178	52		
Anti-PSC ≥ 2.0 µg/mL [Month 0] (N= 176; 55)	10	6		
Anti-PSC ≥ 2.0 µg/mL [Month 1] (N= 180; 55)	176	53		
Anti-PSW-135 ≥ 2.0 µg/mL [Month 0] (N= 176; 58)	3	0		
Anti-PSW-135 ≥ 2.0 µg/mL [Month 1] (N= 178; 58)	146	48		
Anti-PSY ≥ 2.0 µg/mL [Month 0] (N= 175; 58)	10	2		
Anti-PSY ≥ 2.0 µg/mL [Month 1] (N= 180; 55)	172	51		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Tetanus toxoid (TT) antibody concentrations

End point title	Anti-Tetanus toxoid (TT) antibody concentrations[10]

End point description:

Prior to and 1 month after vaccination with Nimenrix vaccine (Months 0 and 1)

End point type	Secondary

End point timeframe:

Prior to and 1 month after vaccination with Nimenrix vaccine (Months 0 and 1)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	355	114		
Units: International Units per milliliter				
geometric mean (confidence interval 95%)				
Month 0 (N= 312; 114)	0.8 (0.692 to 0.926)	1.02 (0.795 to 1.308)		
Month 1 (N= 355; 112)	16.794 (15.318 to 18.411)	17.252 (14.603 to 20.381)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-tetanus toxoid antibody concentrations above the pre-defines cut-off value

End point title	Number of subjects with anti-tetanus toxoid antibody concentrations above the pre-defines cut-off value[11]

End point description:

The cut-off value assessed was greater than or equal to 0.1 International Units per milliliter (IU/mL).

End point type	Secondary

End point timeframe:

Prior to and 1 month after vaccination with Nimenrix vaccine (Months 0 and 1)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	355	114		
Units: Subjects				
Month 0 (N= 312; 114)	293	111		
Month 1 (N= 355; 112)	354	112		

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers at Month 7

End point title	rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers at Month 7[12]

End point description:

The rSBA titers were expressed as geometric mean titers.

End point type	Secondary

End point timeframe:

At Month 7

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	112		
Units: Titer				
geometric mean (confidence interval 95%)				
rSBA-MenA (N= 332; 108)	2121.6 (1913.5 to 2352.2)	2298.3 (1909 to 2767)		
rSBA-MenC (N= 334; 112)	952.4 (826.2 to 1097.8)	1053.9 (803.1 to 1382.9)		
rSBA-MenW-135 (N= 334; 112)	3283.4 (2998.4 to 3595.4)	3497.7 (3008 to 4067.2)		
rSBA-MenY (N= 334; 112)	4432.7 (4027.4 to 4878.8)	4455.6 (3821.4 to 5195.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers above predefined cut-off values at Month 7

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers above predefined cut-off values at Month 7[13]

End point description:

The cut-off values assessed were greater than or equal to (≥) 1:8 and ≥ 1:128.

End point type	Secondary

End point timeframe:

At Month 7

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	112		
Units: Subjects				
rSBA-MenA ≥ 1:8 (N= 332; 108)	330	107		
rSBA-MenC ≥ 1:8 (N= 334; 112)	332	110		
rSBA-MenW-135 ≥ 1:8 (N= 334; 112)	334	112		
rSBA-MenY ≥ 1:8 (N= 334; 112)	333	112		
rSBA-MenA ≥ 1:128 (N= 332; 108)	329	107		
rSBA-MenC ≥ 1:128 (N= 334; 112)	318	108		
rSBA-MenW-135 ≥ 1:128 (N= 334; 112)	333	112		
rSBA-MenY ≥ 1:128 (N= 334; 112)	332	112		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY antibody concentrations at Month 7

End point title	Anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY antibody concentrations at Month 7[14]

End point description:

Concentrations were provided as Geometric Mean Concentrations expressed as micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Month 7

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	167	56		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA (N= 163; 56)	4.14 (3.34 to 5.15)	3.88 (2.44 to 6.16)		
Anti-PSC (N= 164; 56)	3.28 (2.6 to 4.14)	4.15 (2.59 to 6.67)		
Anti-PSW-135 (N= 167; 56)	2.46 (1.99 to 3.05)	3.08 (2.11 to 4.5)		
Anti-PSY (N= 161; 54)	3.76 (2.95 to 4.78)	4.28 (2.9 to 6.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY antibody concentrations above pre-defined cut-off values at Month 7

End point title	Number of subjects with anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY antibody concentrations above pre-defined cut-off values at Month 7[15]

End point description:

The cut-off values assessed include greater than or equal to (≥) 0.3 micrograms per milliliter (µg/mL) and ≥ 2.0 µg/mL.

End point type	Secondary

End point timeframe:

At Month 7

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	167	56		
Units: Subjects				
Anti-PSA ≥ 0.3 µg/mL (N= 163; 56)	160	52		
Anti-PSC ≥ 0.3 µg/mL (N= 164; 56)	157	52		
Anti-PSW-135 ≥ 0.3 µg/mL (N= 167; 56)	157	51		
Anti-PSY ≥ 0.3 µg/mL (N= 161; 54)	154	53		
Anti-PSA ≥ 2.0 µg/mL (N= 163; 56)	110	34		
Anti-PSC ≥ 2.0 µg/mL (N= 164; 56)	94	35		
Anti-PSW-135 ≥ 2.0 µg/mL (N= 167; 56)	93	41		
Anti-PSY ≥ 2.0 µg/mL (N= 161; 54)	104	37		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunoglobulin G (IgG) anti-HAV antibody concentrations

End point title	Immunoglobulin G (IgG) anti-HAV antibody concentrations[16]

End point description:

Concentrations are given as Geomatric Mean Concentrations expressed as milli-Internatinal Units per Milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

Prior to the first dose (Month 0) and 1 month after the third dose of Twinrix vaccine (Month 7)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received hepatitis vaccination (Twinrix).

End point values	Nimenrix + Twinrix Group	Twinrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	99		
Units: milli-Internatinal Units per Milliliter				
geometric mean (confidence interval 95%)				
Month 0 (N= 333; 99)	7.9 (7.6 to 8.1)	7.6 (7.4 to 7.9)		
Month 7 (N= 331; 97)	5876.7 (5362.9 to 6439.8)	6739 (5757.4 to 7887.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with IgG anti-HAV antibody concentrations above the pre-defined cut-off value

End point title	Number of subjects with IgG anti-HAV antibody concentrations above the pre-defined cut-off value[17]

End point description:

The cut-off value assessed was greater than or equal to 15 milli-Internatinal Units per Milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

Prior to the first dose (Month 0) and 1 month after the third dose of Twinrix vaccine (Month 7)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received hepatitis vaccination (Twinrix).

End point values	Nimenrix + Twinrix Group	Twinrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	99		
Units: Subjects				
Month 0 (N= 333; 99)	10	2		
Month 7 (N= 331; 97)	331	97		

Statistical analyses

No statistical analyses for this end point

Secondary: IgG anti-HBs antibody concentrations

End point title	IgG anti-HBs antibody concentrations[18]

End point description:

Concentrations are given as Geomatric Mean Concentrations expressed as milli-Internatinal Units per Milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

Prior to the first dose (Month 0) and 1 month after the third dose of Twinrix vaccine (Month 7)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received hepatitis vaccination (Twinrix).

End point values	Nimenrix + Twinrix Group	Twinrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	100		
Units: milli-Internatinal Units per Milliliter				
geometric mean (confidence interval 95%)				
Month 0 (N= 333; 100)	1.7 (1.6 to 1.7)	1.7 (1.6 to 1.8)		
Month 7 (N= 330; 97)	6088.2 (4977.5 to 7446.7)	7654.7 (5518.8 to 10617.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with IgG anti-HB antibody concentrations above the pre-defined cut-off value

End point title	Number of subjects with IgG anti-HB antibody concentrations above the pre-defined cut-off value[19]

End point description:

The cut-off value assessed was greater than or equal to 10 milli-Internatinal Units per Milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

Prior to the first dose (Month 0) and 1 month after the third dose of Twinrix vaccine (Month 7)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received hepatitis vaccination (Twinrix).

End point values	Nimenrix + Twinrix Group	Twinrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	100		
Units: Subjects				
Month 0 (N= 333; 100)	1	0		
Month 7 (N= 330; 97)	327	97		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited local symptoms post-meningococcal vaccination

End point title	Number of subjects reporting any solicited local symptoms post-meningococcal vaccination[20]

End point description:

Solicited local symptoms assessed include pain, redness and swelling.

End point type	Secondary

End point timeframe:

During a 4-day period after Nimenrix vaccination

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was made only for subjects who received meningitis vaccination (Nimenrix).

End point values	Nimenrix + Twinrix Group	Nimenrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	365	119		
Units: Subjects				
Pain	181	58		
Redness	75	19		
Swelling	71	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited local symptoms post-Twinrix vaccination

End point title	Number of subjects reporting any solicited local symptoms post-Twinrix vaccination[21]

End point description:

Solicited local symptoms assessed include pain, redness and swelling.

End point type	Secondary

End point timeframe:

During a 4-day period after each Twinrix vaccination

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This analysis was made only for subjects who received hepatitis vaccination (Twinrix).

End point values	Nimenrix + Twinrix Group	Twinrix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	122		
Units: Subjects				
Pain	228	73		
Redness	63	19		
Swelling	49	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited general symptoms

End point title	Number of subjects reporting any solicited general symptoms

End point description:

Solicited general symptoms assessed include fatigue, fever (axillary temperature greater than or equal to 37.5 degrees Celcius), gastrointestinal symptoms and headache.

End point type	Secondary

End point timeframe:

During a 4-day period after any vaccination

End point values	Nimenrix + Twinrix Group	Nimenrix Group	Twinrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	366	119	122	
Units: Subjects				
Fatigue	149	30	48	
Fever	17	1	4	
Gastrointestinal symptoms	72	10	23	
Headache	126	26	48	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs)

End point title	Number of subjects reporting any unsolicited adverse events (AEs)

End point description:

Unsolicited AE covers any AE 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.

End point type	Secondary

End point timeframe:

Up to 1 month after each vaccine dose

End point values	Nimenrix + Twinrix Group	Nimenrix Group	Twinrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	367	122	122	
Units: Subjects				
Post Dose 1	62	13	18	
Post Dose 2	26	0	7	
Post Dose 3	52	0	16	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any specific AEs of new onset of chronic illnesses

End point title	Number of subjects reporting any specific AEs of new onset of chronic illnesses

End point description:

Specific AEs of new onset of chronic illnesses include e.g. autoimmune disorders, asthma, type I diabetes and allergies.

End point type	Secondary

End point timeframe:

During the entire study (up to Month 7)

End point values	Nimenrix + Twinrix Group	Nimenrix Group	Twinrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	367	122	122	
Units: Subjects				
Subjects	5	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any rash

End point title	Number of subjects reporting any rash

End point description:

Rashes include e.g. hives, idiopathic thrombocytopenic purpura, petechiae.

End point type	Secondary

End point timeframe:

During the entire study (up to Month 7)

End point values	Nimenrix + Twinrix Group	Nimenrix Group	Twinrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	367	122	122	
Units: Subjects				
Subjects	5	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any conditions prompting emergency room visits

End point title	Number of subjects reporting any conditions prompting emergency room visits

End point description:

End point type	Secondary

End point timeframe:

During the entire study (up to Month 7)

End point values	Nimenrix + Twinrix Group	Nimenrix Group	Twinrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	367	122	122	
Units: Subjects				
Subjects	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events (SAEs)

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

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

During the entire study (up to Month 7)

End point values	Nimenrix + Twinrix Group	Nimenrix Group	Twinrix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	367	122	122	
Units: Subjects				
Subjects	4	0	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events were reported throughout the entire study period (up to Month 7). Unsolicited Adverse Events (AE) were reported up to one month after each vaccine dose.

Adverse event reporting additional description:

Other Frequent (non-serious) Adverse Events were reported only for those subjects who received the vaccination and completed their symptom sheet.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Nimenrix + Twinrix Group

Reporting group description:

Subjects received 1 dose of Nimenrix™ vaccine at Month 0 and 1 dose of Twinrix™ vaccine at Months 0, 1 and 6.

Reporting group title	Nimenrix Group

Reporting group description:

Subjects received 1 dose of Nimenrix™ vaccine at Month 0.

Reporting group title	Twinrix Group

Reporting group description:

Subjects received 1 dose of Twinrix™ vaccine at Months 0, 1 and 6.

Serious adverse events	Nimenrix + Twinrix Group	Nimenrix Group	Twinrix Group
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 367 (1.09%)	0 / 122 (0.00%)	1 / 122 (0.82%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Brain contusion			
subjects affected / exposed	0 / 367 (0.00%)	0 / 122 (0.00%)	1 / 122 (0.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 367 (0.27%)	0 / 122 (0.00%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug toxicity			

subjects affected / exposed	1 / 367 (0.27%)	0 / 122 (0.00%)	0 / 122 (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
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	1 / 367 (0.27%)	0 / 122 (0.00%)	0 / 122 (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
Syncope			
subjects affected / exposed	1 / 367 (0.27%)	0 / 122 (0.00%)	0 / 122 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 367 (0.27%)	0 / 122 (0.00%)	0 / 122 (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

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

Non-serious adverse events	Nimenrix + Twinrix Group	Nimenrix Group	Twinrix Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	228 / 367 (62.13%)	58 / 122 (47.54%)	73 / 122 (59.84%)
General disorders and administration site conditions			
Pain at the injection site (Solicited Symptom)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	181 / 365 (49.59%)	58 / 119 (48.74%)	0 / 122 (0.00%)
occurrences (all)	181	58	0
Swelling at the injection site (Solicited Symptom)			
alternative assessment type: Systematic			
subjects affected / exposed[2]	71 / 365 (19.45%)	18 / 119 (15.13%)	0 / 122 (0.00%)
occurrences (all)	71	18	0
Redness at the injection site (Solicited Symptom)			

alternative assessment type: Systematic			
subjects affected / exposed[3]	75 / 365 (20.55%)	19 / 119 (15.97%)	0 / 122 (0.00%)
occurrences (all)	75	19	0
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed[4]	149 / 366 (40.71%)	30 / 119 (25.21%)	48 / 122 (39.34%)
occurrences (all)	149	30	48
Gastrointestinal symptoms			
alternative assessment type: Systematic			
subjects affected / exposed[5]	72 / 366 (19.67%)	10 / 119 (8.40%)	23 / 122 (18.85%)
occurrences (all)	72	10	23
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[6]	126 / 366 (34.43%)	26 / 119 (21.85%)	48 / 122 (39.34%)
occurrences (all)	126	26	48
Pain at the injection site (AE)			
alternative assessment type: Systematic			
subjects affected / exposed	228 / 367 (62.13%)	0 / 122 (0.00%)	73 / 122 (59.84%)
occurrences (all)	228	0	73
Swelling at the injection site (AE)			
alternative assessment type: Systematic			
subjects affected / exposed	49 / 367 (13.35%)	0 / 122 (0.00%)	19 / 122 (15.57%)
occurrences (all)	49	0	19
Redness at the injection site (AE)			
alternative assessment type: Systematic			
subjects affected / exposed	63 / 367 (17.17%)	0 / 122 (0.00%)	19 / 122 (15.57%)
occurrences (all)	63	0	19

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.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported