Clinical trial results:
A phase IIIb, open, multi-center study to evaluate the immunogenicity, reactogenicity and safety of a booster dose of GSK Biologicals' MenACWY-TT vaccine administered at 6 years post-primary vaccination with either GSK Biologicals' Hib-MenC-TT vaccine (Menitorix™) or Hiberix™ and Meningitec™, in healthy subjects aged 12-18 months at primary vaccination and to evaluate the long-term antibody persistence at 2 and 4 years after MenACWY-TT booster vaccination.

Summary

EudraCT number	2012-002575-34
Trial protocol	Outside EU/EEA
Global end of trial date	20 April 2016

Results information

Result version number	v1
This version publication date	05 November 2016
First version publication date	05 November 2016

Trial information

Trial identification

Sponsor protocol code	116727

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01777308
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 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?	Yes

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	11 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 July 2014
Global end of trial reached?	Yes
Global end of trial date	20 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immunogenicity of MenACWY-TT conjugate vaccine in terms of the percentage of subjects with an rSBA-MenA, rSBA-MenC, rSBA-MenW-135, rSBA-MenY vaccine response*.
*Vaccine response to meningococcal antigens (A, C, W-135 and Y) is defined as:
- For initially seronegative subjects (pre-vaccination rSBA titer below 1:8): rSBA antibody titer ≥ 1:32 one month after vaccination, and
- For initially seropositive subjects (pre-vaccination rSBA titer ≥ 1:8): at least four-fold increase in rSBA titers from pre-vaccination to one month after vaccination.

Protection of trial subjects:

The axillary, rectal, oral or tympanic body temperature of all subjects needed to be measured prior to any study vaccine/product administration. The preferred route for recording temperature in this study was oral. If the subject had fever [fever was defined as temperature ≥ 37.5°C for oral, axillary or tympanic route, or ≥ 38.0°C for rectal route] on the day of vaccination, the vaccination visit was rescheduled within the allowed interval for this visit.
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 for one month (minimum 30 days) following administration of vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 May 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 156
Worldwide total number of subjects	156
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	156
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	Overall study period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Menitorix Group

Arm description:

Healthy male or female subjects who were primed with Menitorix™ vaccine, administered intramuscularly in the deltoid region of the left arm, and Priorix™ vaccine, administered subcutaneously on the upper-right side of the arm, in the primary study HIB-MENC-TT-016 (106445), received one dose of GSK134612 booster vaccine, administered intramuscularly in the deltoid region of the left arm, at Month 72 post primary vaccination (booster visit 1) in the current study.

Arm type	Experimental
Investigational medicinal product name	Priorix™
Investigational medicinal product code	
Other name	MMR
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were primed with one dose of vaccine, administered subcutaneously on the upper-right side of the arm, at 12-18 months of age, during the primary study HIB-MENC-TT-016 (NCT00326118).

Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	Hib-MenC-TT
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were primed with one dose of vaccine, administered intramuscularly in the deltoid region of the left arm, at 12-18 months of age, during the primary study HIB-MENC-TT-016 (NCT00326118).

Investigational medicinal product name	GSK134612
Investigational medicinal product code	
Other name	MenACWY-TT
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were boosted with one dose of vaccine, intramuscularly in the deltoid region of the left arm, at Month 72, post primary vaccination.

Arm title	Hiberix + Meningitec Group

Arm description:

Healthy male or female subjects who were primed with Meningitec™ vaccine, administered

intramuscularly in the deltoid region of the non-dominant arm, Hiberix™ vaccine, administered intramuscularly on the left side of the thigh, and Priorix™ vaccine, administered subcutaneously on the right-upper side of the arm, in the primary study HIB-MENC-TT-016 (106445), received one dose of GSK134612 booster vaccine at Month 72 post primary vaccination (booster visit 1) in the current study.

Arm type	Experimental
Investigational medicinal product name	Meningitec™
Investigational medicinal product code	
Other name	MCC, MenC
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were primed with one dose of vaccine, intramuscularly in the deltoid region of the non-dominant arm, at 12-18 months of age, during the primary study HIB-MENC-TT-016 (NCT00326118).

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

Dosage and administration details:

Subjects were primed with one dose of vaccine, intramuscularly on the left side of the thigh, at 12-18 months of age, during the primary study HIB-MENC-TT-016 (NCT00326118).

Investigational medicinal product name	Priorix™
Investigational medicinal product code	
Other name	MMR
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were primed with one dose of vaccine, subcutaneously on the right-upper side of the arm, at 12-18 months of age, during the primary study HIB-MENC-TT-016 (NCT00326118).

Investigational medicinal product name	GSK134612
Investigational medicinal product code	
Other name	MenACWY-TT
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were boosted with one dose of vaccine, intramuscularly in the deltoid region of the left arm, at Month 72, post primary vaccination.

Number of subjects in period 1	Menitorix Group	Hiberix + Meningitec Group
Started	119	37
Completed	118	37
Not completed	1	0
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Menitorix Group
Reporting group description:	
Healthy male or female subjects who were primed with Menitorix™ vaccine, administered intramuscularly in the deltoid region of the left arm, and Priorix™ vaccine, administered subcutaneously on the upper-right side of the arm, in the primary study HIB-MENC-TT-016 (106445), received one dose of GSK134612 booster vaccine, administered intramuscularly in the deltoid region of the left arm, at Month 72 post primary vaccination (booster visit 1) in the current study.	
Reporting group title	Hiberix + Meningitec Group
Reporting group description:	
Healthy male or female subjects who were primed with Meningitec™ vaccine, administered intramuscularly in the deltoid region of the non-dominant arm, Hiberix™ vaccine, administered intramuscularly on the left side of the thigh, and Priorix™ vaccine, administered subcutaneously on the right-upper side of the arm, in the primary study HIB-MENC-TT-016 (106445), received one dose of GSK134612 booster vaccine at Month 72 post primary vaccination (booster visit 1) in the current study.	

Reporting group values	Menitorix Group	Hiberix + Meningitec Group	Total
Number of subjects	119	37	156
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			
arithmetic mean	7	7	
standard deviation	± 0.2	± 0	-
Gender categorical Units: Subjects			
Female	57	14	71
Male	62	23	85

End points

End points reporting groups

Reporting group title	Menitorix Group

Reporting group description:

Healthy male or female subjects who were primed with Menitorix™ vaccine, administered intramuscularly in the deltoid region of the left arm, and Priorix™ vaccine, administered subcutaneously on the upper-right side of the arm, in the primary study HIB-MENC-TT-016 (106445), received one dose of GSK134612 booster vaccine, administered intramuscularly in the deltoid region of the left arm, at Month 72 post primary vaccination (booster visit 1) in the current study.

Reporting group title	Hiberix + Meningitec Group

Reporting group description:

Healthy male or female subjects who were primed with Meningitec™ vaccine, administered intramuscularly in the deltoid region of the non-dominant arm, Hiberix™ vaccine, administered intramuscularly on the left side of the thigh, and Priorix™ vaccine, administered subcutaneously on the right-upper side of the arm, in the primary study HIB-MENC-TT-016 (106445), received one dose of GSK134612 booster vaccine at Month 72 post primary vaccination (booster visit 1) in the current study.

Primary: Number of subjects with vaccine response to the serum bactericidal assay meningococcal serogroup A, C, W-135 and Y using rabbit complement (rSBA-MenA, rSBA-MenC, rSBA-MenW-135, rSBA-MenY)

End point title	Number of subjects with vaccine response to the serum bactericidal assay meningococcal serogroup A, C, W-135 and Y using rabbit complement (rSBA-MenA, rSBA-MenC, rSBA-MenW-135, rSBA-MenY)[1]

End point description:

Vaccine response was defined as :
- For initially seronegative subjects, antibody titer ≥ 1:32 at post-vaccination, and
- For initially seropositive subjects, antibody titer at post-vaccination ≥ 4 fold the pre-vaccination antibody titer.

End point type	Primary

End point timeframe:

At one month post booster vaccination (Month 73)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	Menitorix Group	Hiberix + Meningitec Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	34		
Units: Subjects				
rSBA-MenA (N=104;34)	102	33		
rSBA-MenC (N=104;34)	101	33		
rSBA-MenW-135 (N=104;34)	102	33		
rSBA-MenY (N=104;34)	101	33		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-rSBA-MenA, anti-rSBA-MenC, anti-rSBA-MenW-135 and anti-rSBA-MenY antibody titers greater than or equal to (≥) the predefined cut-off values of 1:8 and 1:128

End point title	Number of subjects with anti-rSBA-MenA, anti-rSBA-MenC, anti-rSBA-MenW-135 and anti-rSBA-MenY antibody titers greater than or equal to (≥) the predefined cut-off values of 1:8 and 1:128

End point description:

End point type	Secondary

End point timeframe:

At one month post booster vaccination (Month 73)

End point values	Menitorix Group	Hiberix + Meningitec Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	35		
Units: Subjects				
rSBA-MenA, ≥ 1:8 (N=104;35)	102	35		
rSBA-MenA, ≥ 1:128 (N=104;35)	102	35		
rSBA-MenC, ≥ 1:8 (N=104;35)	102	35		
rSBA-MenC, ≥ 1:128 (N=104;35)	102	34		
rSBA-MenW-135, ≥ 1:8 (N=104;35)	102	35		
rSBA-MenW-135, ≥ 1:128 (N=104;35)	102	35		
rSBA-MenY, ≥ 1:8 (N=104;35)	103	34		
rSBA-MenY, ≥ 1:128 (N=104;35)	103	34		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rSBA-MenA, anti-rSBA-MenC, anti-rSBA-MenW-135 and anti-rSBA-MenY antibody titers

End point title	Anti-rSBA-MenA, anti-rSBA-MenC, anti-rSBA-MenW-135 and anti-rSBA-MenY antibody titers

End point description:

End point type	Secondary

End point timeframe:

At one month post booster vaccination (Month 73)

End point values	Menitorix Group	Hiberix + Meningitec Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	35		
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA (N=104;35)	3421.4 (2659.3 to 4402)	2925.1 (1949.5 to 4389)		
rSBA-MenC (N=104;35)	11819.2 (9026.4 to 15476.1)	7419.7 (4543.2 to 12117.3)		
rSBA-MenW-135 (N=104;35)	17166.5 (12745.9 to 23120.3)	15747.7 (10033 to 24717.7)		
rSBA-MenY (N=104;35)	4871 (3932.7 to 6033.1)	3495.9 (2126.6 to 5746.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local and solicited general symptoms

End point title	Number of subjects with solicited local and solicited general symptoms

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Assessed solicited general symptoms were fatigue, gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain), headache, and fever [defined as oral temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

During the 4 days (Day 0-3), post booster vaccination

End point values	Menitorix Group	Hiberix + Meningitec Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	37		
Units: Subjects				
Any Pain (N=118;37)	69	15		
Any Redness (N=118;37)	56	19		
Any Swelling (N=118;37)	30	8		
Any Fatigue (N=118;37)	31	10		
Any Gastrointestinal symptoms (N=118;37)	29	5		
Any Headache (N=118;37)	29	6		
Any Fever (Oral) (N=118;37)	6	1		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reporting new onset chronic illnesses (NOCIs)

End point description:

NOCIs include autoimmune disorders, asthma, type I diabetes, allergies.

End point type	Secondary

End point timeframe:

During the 31 days period (Day 0-30), post booster vaccination

End point values	Menitorix Group	Hiberix + Meningitec Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	37		
Units: Subjects				
Any NOCIs	0	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

During the 31 days period (Day 0-30), post booster vaccination

End point values	Menitorix Group	Hiberix + Meningitec Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	37		
Units: Subjects				
Any AEs	36	7		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

SAEs assessed include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

During the 31 days period (Day 0-30), post booster vaccination

End point values	Menitorix Group	Hiberix + Meningitec Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	37		
Units: Subjects				
Any SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited and unsolicited symptoms at least once

End point title	Number of subjects reporting solicited and unsolicited symptoms at least once

End point description:

End point type	Secondary

End point timeframe:

Within the 31-day (Days 0-30) post booster vaccination

End point values	Menitorix Group	Hiberix + Meningitec Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	37		
Units: Subjects				
Any solicited/unsolicited symptoms	97	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with SAEs

End point title	Number of subjects with SAEs

End point description:

SAEs assessed include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

From Month 72 until Data Lock Point (DLP) August 30th 2016

End point values	Menitorix Group	Hiberix + Meningitec Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	37		
Units: Subjects				
Any SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and solicited general symptoms: during the 4-day post-vaccination period; Solicited and unsolicited symptoms: during the 31-day post-vaccination period; SAEs: during the 31-day post-vaccination period and up to DLP.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Menitorix Group

Reporting group description:

Healthy male or female subjects who were primed with Menitorix™ vaccine, administered intramuscularly in the deltoid region of the left arm, and Priorix™ vaccine, administered subcutaneously on the upper-right side of the arm, in the primary study HIB-MENC-TT-016 (106445), received one dose of GSK134612 booster vaccine, administered intramuscularly in the deltoid region of the left arm, at Month 72 post primary vaccination (booster visit 1) in the current study.

Reporting group title	Hiberix + Meningitec Group

Reporting group description:

Healthy male or female subjects who were primed with Meningitec™ vaccine, administered intramuscularly in the deltoid region of the non-dominant arm, Hiberix™ vaccine, administered intramuscularly on the left side of the thigh, and Priorix™ vaccine, administered subcutaneously on the right-upper side of the arm, in the primary study HIB-MENC-TT-016 (106445), received one dose of GSK134612 booster vaccine at Month 72 post primary vaccination (booster visit 1) in the current study.

Serious adverse events	Menitorix Group	Hiberix + Meningitec Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 119 (0.00%)	0 / 37 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Menitorix Group	Hiberix + Meningitec Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 119 (57.98%)	19 / 37 (51.35%)	
Nervous system disorders			
Headache (unsolicited)			
subjects affected / exposed	30 / 119 (25.21%)	7 / 37 (18.92%)	
occurrences (all)	30	9	
General disorders and administration			

site conditions			
Fatigue (unsolicited)			
subjects affected / exposed	31 / 119 (26.05%)	10 / 37 (27.03%)	
occurrences (all)	31	10	
Pain (unsolicited)			
subjects affected / exposed	69 / 119 (57.98%)	15 / 37 (40.54%)	
occurrences (all)	69	15	
Pyrexia			
subjects affected / exposed	6 / 119 (5.04%)	2 / 37 (5.41%)	
occurrences (all)	6	2	
Swelling (unsolicited)			
subjects affected / exposed	30 / 119 (25.21%)	8 / 37 (21.62%)	
occurrences (all)	30	8	
Pain (solicited)			
subjects affected / exposed[1]	69 / 118 (58.47%)	15 / 37 (40.54%)	
occurrences (all)	69	15	
Redness			
subjects affected / exposed[2]	56 / 118 (47.46%)	19 / 37 (51.35%)	
occurrences (all)	56	19	
Swelling (solicited)			
subjects affected / exposed[3]	30 / 118 (25.42%)	8 / 37 (21.62%)	
occurrences (all)	30	8	
Fatigue (solicited)			
subjects affected / exposed[4]	31 / 118 (26.27%)	10 / 37 (27.03%)	
occurrences (all)	31	10	
Gastrointestinal symptoms			
subjects affected / exposed[5]	29 / 118 (24.58%)	5 / 37 (13.51%)	
occurrences (all)	29	5	
Headache (solicited)			
subjects affected / exposed[6]	29 / 118 (24.58%)	6 / 37 (16.22%)	
occurrences (all)	29	6	
Fever (Oral)			
subjects affected / exposed[7]	6 / 118 (5.08%)	1 / 37 (2.70%)	
occurrences (all)	6	1	
Gastrointestinal disorders			

Gastrointestinal disorder subjects affected / exposed occurrences (all)	29 / 119 (24.37%) 29	5 / 37 (13.51%) 5	
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	56 / 119 (47.06%) 56	19 / 37 (51.35%) 19	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	7 / 119 (5.88%) 7	2 / 37 (5.41%) 2	

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.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2013	This protocol amendment has been done to remove the recording of any antipyretic administered in the period starting 6 hours before vaccination and ending 12 hours after vaccination in the protocol, since the collection of this information is not needed for the study, is not included in the eCRF and also involves a complex collection process. In addition: • Table 5 has been corrected with an error with respect to the allowed interval at Year 4. • The authors list has been updated according to changes in the clinical study team. • The Sponsor Information section now mentions that the Sponsor Information Sheet will be used instead of the local study contact information document for details of the Medical Expert and Study Monitor. • The duration of the study of approximately four years for each subject has been mentioned for more clarity. • The introduction has been updated with the current licensing status of GSK Biologicals' MenACWY-TT conjugate vaccine. • The recording of subjects' non-participation in the booster study in the eCRF has been removed. • The name of the HPA (Health Protection Agency) laboratory is now changed to PHE (Public Health England) laboratory. • The manner in which the investigators will be provided with the immunogenicity results has been updated. • The preparation of an annex report after the Year 2 persistence analysis has been removed since this analysis will be included in the Year 4 persistence CSR only.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported