



Clinical trial results:

A Multicenter Post Marketing Surveillance Study to monitor the safety of GlaxoSmithKline (GSK) Biologicals' Meningococcal ACWY conjugate vaccine(MenACWY-CRM) administered according to the prescribing information to healthy subjects from 2 months to 55 years of age in the Republic of South Korea.

Summary

EudraCT number	2017-000166-30
Trial protocol	Outside EU/EEA
Global end of trial date	22 January 2018

Results information

Result version number	v1 (current)
This version publication date	05 August 2018
First version publication date	05 August 2018

Trial information

Trial identification

Sponsor protocol code	205341
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 January 2018
Global end of trial reached?	Yes
Global end of trial date	22 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to monitor the safety of MenACWY-CRM vaccine in subjects from 2 months to 55 years of age, as evaluated by:

- Local and systemic solicited adverse events reported from study Day 1 (day of vaccination) through study Day 7 post-vaccination;
- All unsolicited Adverse Events (AEs) reported from study Day 1 (day of vaccination) through study Day 7 post-vaccination;
- Medically attended Adverse Events reported from study Day 1 to study termination (Day 29/early termination).
- All Serious Adverse Events (SAEs) reported from study Day 1 to study termination (Day 29/early termination).

Protection of trial subjects:

All subjects were observed closely for at least 30 minutes in the clinic after vaccination, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines. Study vaccines were administered only by personnel qualified to perform that function according to the routine clinical practice and under applicable local laws and regulations for the specific study site.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 March 2013
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	Korea, Republic of: 3948
Worldwide total number of subjects	3948
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	654

months)	
Children (2-11 years)	955
Adolescents (12-17 years)	302
Adults (18-64 years)	2035
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy subjects from 2 months to 55 years of age were enrolled in 46 centres in South Korea.

Pre-assignment

Screening details:

Out of the 3,948 subjects enrolled, only 3,939 subjects were exposed to vaccination as 1 subject did not receive a study vaccination and 8 subjects did not provide post vaccination safety data. Among 3939 subjects, 15 subjects are in the ≥ 56 age category (outside the range defined as per the protocol).

Pre-assignment period milestones

Number of subjects started	3948
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Number of subjects completed	3939
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Pre-assignment subject non-completion reasons

Reason: Number of subjects	No safety data provided: 8
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Reason: Number of subjects	Did not receive study vaccination: 1
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Period 1

Period 1 title	Overall Study (overall period)
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Is this the baseline period?	Yes
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Allocation method	Not applicable
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Blinding used	Not blinded
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Blinding implementation details:

This was an open- label study. No blinding methods were used

Arms

Arm title	MenACWY-CRM Group
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Arm description:

Healthy subjects from 2 months to 55 years of age in South Korea, who received MenACWY-CRM (Menveo) vaccination, according to routine clinical care.

Arm type	Safety surveillance
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Investigational medicinal product name	MenACWY-CRM conjugate vaccine (Menveo)
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Solution for injection
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Routes of administration	Intramuscular use
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Dosage and administration details:

one intramuscular injection of MenACWY-CRM vaccine at Day 1

Number of subjects in period 1^[1]	MenACWY-CRM Group
Started	3939
Completed	3888
Not completed	51
Consent withdrawn by subject	22
Inappropriate enrollment	18
Lost to follow-up	10
withdrawal and inappropriate enrollment	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: The number of subjects reported in the baseline period are based on the exposed set (3939). Out of 3948 subjects enrolled, 8 subjects did not report safety data and 1 subject did not receive the study vaccination.

Baseline characteristics

Reporting groups

Reporting group title	MenACWY-CRM Group
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Reporting group description:

Healthy subjects from 2 months to 55 years of age in South Korea, who received MenACWY-CRM (Menveo) vaccination, according to routine clinical care.

Reporting group values	MenACWY-CRM Group	Total	
Number of subjects	3939	3939	
Age categorical			
Units: Subjects			
2- 23 months	654	654	
2-5 years	551	551	
6-10 years	339	339	
11-18 years	433	433	
19-34 years	1286	1286	
35 - 55 years	661	661	
≥ 56 years	15	15	
Age continuous			
Units: years			
log mean	18.37		
standard deviation	± 15.40	-	
Gender categorical			
Units: Subjects			
Female	2181	2181	
Male	1758	1758	
Race/Ethnicity, Customized			
Units: Subjects			
Asian	3937	3937	
Caucasian	1	1	
Hispanic	1	1	

End points

End points reporting groups

Reporting group title	MenACWY-CRM Group
Reporting group description:	
Healthy subjects from 2 months to 55 years of age in South Korea, who received MenACWY-CRM (Menveo) vaccination, according to routine clinical care.	

Primary: Number of subjects reporting any local and systemic solicited Adverse Events (AEs)

End point title	Number of subjects reporting any local and systemic solicited Adverse Events (AEs) ^[1]
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End point description:

Assessed solicited local AEs include: injection site erythema, injection site induration, injection site tenderness, injection site pain. Assessed solicited systemic AEs include: change in eating habits, sleepiness, irritability, rash, vomiting, diarrhea, fever, chills, nausea, malaise, generalized myalgia, generalized arthralgia, headache. "Any" is defined as any report of the specified symptom irrespective of intensity grade. Subjects from 2 months to 55 years of age were evaluated for the outcome measure. This analysis was performed on the Safety per protocol set, which included all enrolled subjects who signed an informed consent, underwent screening, received a subject number, received a study vaccination and provided post vaccination data, excluding 19 subjects from safety set with protocol violations.

End point type	Primary
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End point timeframe:

From Day 1 (day of vaccination) to Day 7 post vaccination

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 endpoint was descriptive analysis. Therefore, no statistical analyses have been specified for this endpoint.

End point values	MenACWY-CRM Group			
Subject group type	Reporting group			
Number of subjects analysed	3920			
Units: Participants				
Any injection site tenderness, 2 - 23 months(N-653)	67			
Any injection site erythema, 2 - 23 months(N-653)	32			
Any injection site induration, 2 - 23 months(N-653)	28			
Any change in eating habits, 2 - 23 months(N-653)	110			
Any sleepiness, 2 - 23 months(N-653)	126			
Any irritability, 2 - 23 months(N-653)	219			
Any vomiting, 2 - 23 months(N-653)	66			
Any diarrhea, 2 - 23 months(N-653)	82			
Any rash, 2 - 23 months(N-653)	20			
Any fever, 2 - 23 months(N-653)	57			
Any injection site tenderness, 2 - 5 years(N-551)	135			
Any injection site erythema, 2 - 5 years(N-551)	71			

Any injection site induration, 2 - 5 years(N-551)	49			
Any change in eating habits, 2 - 5 years(N-551)	22			
Any sleepiness, 2 - 5 years(N-551)	17			
Any irritability, 2 - 5 years(N-551)	35			
Any vomiting, 2 - 5 years(N-551)	4			
Any diarrhea, 2 - 5 years(N-551)	7			
Any rash, 2 - 5 years(N-551)	18			
Any fever, 2 - 5 years(N-551)	12			
Any injection site tenderness, 6 - 10 years(N-338)	108			
Any injection site erythema, 6 - 10 years(N-338)	53			
Any injection site induration, 6 - 10 years(N-338)	45			
Any chills, 6 - 10 years(N-338)	7			
Any nausea, 6 - 10 years(N-338)	7			
Any malaise, 6 - 10 years(N-338)	5			
Any myalgia, 6 - 10 years(N-338)	6			
Any arthralgia, 6 - 10 years(N-338)	6			
Any headache, 6 - 10 years(N-338)	11			
Any rash, 6 - 10 years(N-338)	10			
Any fever, 6 - 10 years(N-338)	9			
Any injection site tenderness, 11-18 years(N-431)	91			
Any injection site erythema, 11 - 18 years(N-431)	17			
Any injection site induration, 11- 18 years(N-431)	21			
Any chills, 11 - 18 years(N-431)	9			
Any nausea, 11 - 18 years(N-431)	4			
Any malaise, 11 - 18 years(N-431)	9			
Any myalgia, 11 - 18 years(N-431)	12			
Any arthralgia, 11 - 18 years(N-431)	5			
Any headache, 11 - 18 years(N-431)	12			
Any rash, 11 - 18 years(N-431)	6			
Any fever, 11 - 18 years(N-431)	4			
Any injection site tenderness,19-34 years(N-1286)	214			
Any injection site erythema, 19 - 34 years(N-1286)	14			
Any injection site induration,19 - 34 years(N-1286)	9			
Any chills, 19 - 34 years(N-1286)	7			
Any nausea, 19 - 34 years(N-1286)	6			
Any malaise, 19 - 34 years(N-1286)	20			
Any myalgia, 19 - 34 years(N-1286)	21			
Any arthralgia, 19 - 34 years(N-1286)	8			
Any headache, 19 - 34 years(N-1286)	29			
Any rash, 19 - 34 years(N-1286)	13			
Any fever, 19 - 34 years(N-1286)	3			
Any injection site tenderness, 35-55 years(N-661)	174			
Any injection site erythema, 35 - 55 years(N-661)	7			

Any injection site induration, 35 -55 years(N-661)	6			
Any chills, 35 - 55 years(N-661)	7			
Any nausea, 35 - 55 years(N-661)	9			
Any malaise, 35 - 55 years(N-661)	16			
Any myalgia, 35 - 55 years(N-661)	23			
Any arthralgia, 35 - 55 years(N-661)	15			
Any headache, 35 - 55 years(N-661)	19			
Any rash, 35 - 55 years(N-661)	6			
Any fever, 35 - 55 years(N-661)	2			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reporting any unsolicited adverse events (AEs) ^[2]
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End point description:

An AE is defined as any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product at any dose that does not necessarily have to have a causal relationship with this treatment. All unsolicited AEs reported from day 1 to day 7 post vaccination were assessed. "Any" is defined as any report of the specified symptom irrespective of intensity grade. Subjects from 2 months to 55 years of age were evaluated for the outcome measure. This analysis was performed on the Safety per protocol set, which included all enrolled subjects who signed an informed consent, underwent screening, received a subject number, received a study vaccination and provided post vaccination data, excluding 19 subjects from safety set with protocol violations.

End point type	Primary
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End point timeframe:

From Day 1 (day of vaccination) to Day 7 post vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this endpoint was descriptive analysis. Therefore, no statistical analyses have been specified for this endpoint.

End point values	MenACWY-CRM Group			
Subject group type	Reporting group			
Number of subjects analysed	3920			
Units: Participants				
2 - 23 Months(N-653)	82			
2 - 5 Years(N-551)	56			
6 - 10 Years(N-338)	18			
11 - 18 Years(N-431)	8			
19 - 34 Years(N-1286)	17			
35 - 55 Years(N-661)	5			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting medically attended AEs (MAAEs)

End point title	Number of subjects reporting medically attended AEs
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End point description:

MAAEs are defined as events that require a physician's visit or an emergency room visit. All reported MAAEs from day 1 to day 29 were assessed. Subjects from 2 months to 55 years of age were evaluated for the outcome measure.

This analysis was performed on the Safety per protocol set, which included all enrolled subjects who signed an informed consent, underwent screening, received a subject number, received a study vaccination and provided post vaccination data, excluding 19 subjects from safety set with protocol violations.

End point type	Primary
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End point timeframe:

From Day 1 (day of vaccination) to study termination (Day 29/early termination)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this endpoint was descriptive analysis. Therefore, no statistical analyses have been specified for this endpoint.

End point values	MenACWY-CRM Group			
Subject group type	Reporting group			
Number of subjects analysed	3920			
Units: Participants				
2 - 23 Months(N-653)	238			
2 - 5 Years(N-551)	120			
6 - 10 Years(N-338)	28			
11 - 18 Years(N-431)	20			
19 - 34 Years(N-1286)	16			
35 - 55 Years(N-661)	5			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting serious AEs (SAEs)

End point title	Number of subjects reporting serious AEs (SAEs) ^[4]
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End point description:

SAE is defined as any untoward medical occurrence that at any dose results in death, is life-threatening; it does not refer to an event which hypothetically might have caused death if it were more severe, requires or prolongs subject's hospitalization, results in persistent/significant disability/incapacity, results in congenital anomaly/birth defect, is an important and significant medical event that may not be immediately life threatening/resulting in death/hospitalization but, based upon appropriate medical judgment, may jeopardize the subject/may require intervention to prevent one of the other outcomes listed above. Subjects from 2 months to 55 years of age were evaluated for the outcome measure.

This analysis was performed on the Safety per protocol set, which included all enrolled subjects who signed an informed consent, underwent screening, received a subject number, received a study vaccination & provided post vaccination data, excluding 19 subjects from safety set with protocol

End point type	Primary
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End point timeframe:

From Day 1 (day of vaccination) to study termination (Day 29/early termination)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this endpoint was descriptive analysis. Therefore, no statistical analyses have been specified for this endpoint.

End point values	MenACWY-CRM Group			
Subject group type	Reporting group			
Number of subjects analysed	3920			
Units: Participants				
2 - 23 Months(N-653)	3			
2 - 5 Years(N-551)	3			
6 - 10 Years(N-338)	0			
11 - 18 Years(N-431)	2			
19 - 34 Years(N-1286)	0			
35 - 55 Years(N-661)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited and unsolicited AEs were reported from Day 1 to Day 7. MAAEs and SAEs were reported from study day 1 to study termination (Day 29/early termination).

Adverse event reporting additional description:

Total number of subjects at risk for SAEs, all cause mortality and FAEs were analyzed from the Safety set (including 15 subjects of ≥ 56 years age category).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	MenACWY-CRM Group
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Reporting group description:

Healthy subjects from 2 months to 55 years of age in South Korea, who received MenACWY-CRM (Menveo) vaccination, according to routine clinical care.

Serious adverse events	MenACWY-CRM Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 3939 (0.20%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pneumonia			
subjects affected / exposed	4 / 3939 (0.10%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	MenACWY-CRM Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1379 / 3939 (35.01%)		
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Orthostatic hypotension-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site pain-Solicited Local AE	Additional description: This symptom was assessed as a solicited local AE.		
subjects affected / exposed	592 / 3939 (15.03%)		
occurrences (all)	592		
Injection site tenderness-Solicited local AE	Additional description: This symptom was assessed as a solicited local AE.		
subjects affected / exposed	202 / 3939 (5.13%)		
occurrences (all)	202		
Injection site erythema-Solicited local AE	Additional description: This symptom was assessed as a solicited local AE.		
alternative assessment type: Non-systematic			
subjects affected / exposed	195 / 3939 (4.95%)		
occurrences (all)	195		
Injection site induration-solicited local AE	Additional description: This symptom was assessed as a solicited local AE.		

subjects affected / exposed occurrences (all)	158 / 3939 (4.01%) 158		
Diarrhea-solicited general AE	Additional description: This symptom was assessed as a solicited general AE.		
subjects affected / exposed occurrences (all)	89 / 3939 (2.26%) 89		
Chills-solicited general AE	Additional description: This symptom was assessed as a solicited general AE.		
subjects affected / exposed occurrences (all)	31 / 3939 (0.79%) 31		
Nausea-solicited general AE	Additional description: This symptom was assessed as a solicited general AE.		
subjects affected / exposed occurrences (all)	28 / 3939 (0.71%) 28		
Myalgia-solicited general AE	Additional description: This symptom was assessed as a solicited general AE.		
subjects affected / exposed occurrences (all)	64 / 3939 (1.62%) 64		
Malaise-solicited general AE	Additional description: This symptom was assessed as a solicited general AE,		
subjects affected / exposed occurrences (all)	53 / 3939 (1.35%) 53		
Arthralgia-solicited general AE	Additional description: This symptom was assessed as a solicited general AE.		
subjects affected / exposed occurrences (all)	34 / 3939 (0.86%) 34		
Fever-solicited general AE	Additional description: This symptom was assessed as a solicited general AE.		
subjects affected / exposed occurrences (all)	87 / 3939 (2.21%) 87		
Pyrexia			
subjects affected / exposed occurrences (all)	8 / 3939 (0.20%) 8		
Injection site erythema			
subjects affected / exposed occurrences (all)	9 / 3939 (0.23%) 9		
Injection site induration			
subjects affected / exposed occurrences (all)	7 / 3939 (0.18%) 7		
Injection site pruritus			
subjects affected / exposed occurrences (all)	7 / 3939 (0.18%) 7		
Injection site pain			

subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Injection site warmth			
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Chest pain			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Injection site bruising			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Injection site swelling			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Pyrexia-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	15 / 3939 (0.38%)		
occurrences (all)	17		
Injection site erythema-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Injection site pruritus-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Oedema peripheral-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Chest pain-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Injection site rash-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Injection site swelling-MAAE	Additional description: This symptom was assessed as a MAAE.		

subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Immune system disorders Atopy alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Reproductive system and breast disorders Prostatic cyst subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Prostatic cyst-MAAE subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Additional description: This symptom was assessed as a MAAE.			
Respiratory, thoracic and mediastinal disorders Rhinitis allergic subjects affected / exposed occurrences (all)	6 / 3939 (0.15%) 6		
Asthma subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Cough subjects affected / exposed occurrences (all)	4 / 3939 (0.10%) 4		
Rhinorrhoea subjects affected / exposed occurrences (all)	2 / 3939 (0.05%) 2		
Nasal congestion subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Productive cough subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Rhinitis allergic-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed occurrences (all)	18 / 3939 (0.46%) 18		
Asthma-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed occurrences (all)	8 / 3939 (0.20%) 8		
Cough-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed occurrences (all)	2 / 3939 (0.05%) 2		
Rhinorrhoea-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed occurrences (all)	3 / 3939 (0.08%) 3		
Nasal congestion-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed occurrences (all)	2 / 3939 (0.05%) 2		
Productive cough-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Psychiatric disorders			
Eating disorder-solicited general AE	Additional description: This symptom was assessed as a solicited general AE.		
subjects affected / exposed occurrences (all)	132 / 3939 (3.35%) 132		
Irritability-solicited general AE	Additional description: This symptom was assessed as a solicited general AE.		
subjects affected / exposed occurrences (all)	254 / 3939 (6.45%) 254		
Eating disorder			
subjects affected / exposed occurrences (all)	6 / 3939 (0.15%) 6		
Irritability			
subjects affected / exposed occurrences (all)	4 / 3939 (0.10%) 4		
Eating disorder-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed occurrences (all)	3 / 3939 (0.08%) 3		

Irritability-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.		
	1 / 3939 (0.03%) 1		
Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all) Laceration subjects affected / exposed occurrences (all) Nail injury subjects affected / exposed occurrences (all) Arthropod bite-MAAE subjects affected / exposed occurrences (all) Contusion-MAAE subjects affected / exposed occurrences (all) Laceration-MAAE subjects affected / exposed occurrences (all) Ligament sprain-MAAE subjects affected / exposed occurrences (all) Muscle strain-MAAE subjects affected / exposed occurrences (all) Skin abrasion-MAAE subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
	1 / 3939 (0.03%) 2		
	1 / 3939 (0.03%) 1		
	Additional description: This symptom was assessed as a MAAE.		
	1 / 3939 (0.03%) 1		
	Additional description: This symptom was assessed as a MAAE.		
	2 / 3939 (0.05%) 2		
	Additional description: This symptom was assessed as a MAAE.		
	1 / 3939 (0.03%) 2		
	Additional description: This symptom was assessed as a MAAE.		
	1 / 3939 (0.03%) 1		
	Additional description: This symptom was assessed as a MAAE.		
	1 / 3939 (0.03%) 1		
	Additional description: This symptom was assessed as a MAAE.		
	1 / 3939 (0.03%) 1		
Nervous system disorders Sleepiness-Solicited general AE subjects affected / exposed occurrences (all) Headache-solicited general AE	Additional description: This symptom was assessed as a solicited general AE.		
	143 / 3939 (3.63%) 143		
	Additional description: This symptom was assessed as a solicited general AE.		

subjects affected / exposed	73 / 3939 (1.85%)		
occurrences (all)	73		
Headache			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Burning sensation			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Dizziness-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
sleepiness			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Anaemia-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Iron deficiency anaemia-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Lymphadenitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Eye disorders			

Conjunctivitis allergic subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Eye discharge subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Ocular hyperaemia subjects affected / exposed occurrences (all)	1 / 3939 (0.03%) 1		
Conjunctivitis allergic-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE. 1 / 3939 (0.03%) 1		
Keratitis-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE. 1 / 3939 (0.03%) 1		
Gastrointestinal disorders			
Vomiting-solicited general AE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a solicited general AE. 70 / 3939 (1.78%) 70		
Enteritis subjects affected / exposed occurrences (all)	5 / 3939 (0.13%) 5		
Diarrhoea subjects affected / exposed occurrences (all)	6 / 3939 (0.15%) 6		
Vomiting subjects affected / exposed occurrences (all)	5 / 3939 (0.13%) 5		
Constipation subjects affected / exposed occurrences (all)	2 / 3939 (0.05%) 2		
Stomatitis subjects affected / exposed occurrences (all)	2 / 3939 (0.05%) 2		
Abdominal pain			

subjects affected / exposed	4 / 3939 (0.10%)		
occurrences (all)	4		
Colitis			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Dental caries			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Gastritis erosive			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Enteritis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	22 / 3939 (0.56%)		
occurrences (all)	23		
Diarrhoea-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	7 / 3939 (0.18%)		
occurrences (all)	7		
Vomiting-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	8 / 3939 (0.20%)		
occurrences (all)	8		
Constipation-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	7 / 3939 (0.18%)		
occurrences (all)	7		
Stomatitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	7 / 3939 (0.18%)		
occurrences (all)	7		
Gastritis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	6 / 3939 (0.15%)		
occurrences (all)	6		
Abdominal pain-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Colitis-MAAE	Additional description: This symptom was assessed as a MAAE.		

subjects affected / exposed	3 / 3939 (0.08%)		
occurrences (all)	3		
Chronic gastritis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Dental caries-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Gastritis erosive-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Gastroesophageal reflux disease-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Irritable bowel syndrome-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash-solicited general AE	Additional description: This symptom was assessed as a solicited general AE.		
subjects affected / exposed	74 / 3939 (1.88%)		
occurrences (all)	74		
Dermatitis atopic			
subjects affected / exposed	7 / 3939 (0.18%)		
occurrences (all)	7		
Dermatitis			
subjects affected / exposed	5 / 3939 (0.13%)		
occurrences (all)	5		
Urticaria			
subjects affected / exposed	5 / 3939 (0.13%)		
occurrences (all)	5		
Dermatitis contact			
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Dermatitis allergic			

subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Cold sweat			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Dyshidrotic eczema			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Generalised erythema			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Dermatitis atopic-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	20 / 3939 (0.51%)		
occurrences (all)	20		
Dermatitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	11 / 3939 (0.28%)		
occurrences (all)	11		
Urticaria-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	10 / 3939 (0.25%)		
occurrences (all)	12		
Dermatitis contact-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	8 / 3939 (0.20%)		
occurrences (all)	8		
Blister-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Dermatitis allergic-MAAE	Additional description: This symptom was assessed as a MAAE.		

subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Dermatitis diaper-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Eczema-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Generalised erythema-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Miliaria-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Seborrhoeic dermatitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Renal cyst			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Haematuria-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Renal cyst-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Tubulointerstitial nephritis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		

Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Arthralgia-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Neck pain-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	21 / 3939 (0.53%)		
occurrences (all)	21		
Nasopharyngitis			
subjects affected / exposed	31 / 3939 (0.79%)		
occurrences (all)	31		
Pharyngitis			
subjects affected / exposed	13 / 3939 (0.33%)		
occurrences (all)	13		
Gastroenteritis			
subjects affected / exposed	5 / 3939 (0.13%)		
occurrences (all)	5		
Bronchiolitis			
subjects affected / exposed	11 / 3939 (0.28%)		
occurrences (all)	11		
Otitis media			
subjects affected / exposed	6 / 3939 (0.15%)		
occurrences (all)	6		
Pneumonia			
subjects affected / exposed	3 / 3939 (0.08%)		
occurrences (all)	3		
Rhinitis			
subjects affected / exposed	6 / 3939 (0.15%)		
occurrences (all)	6		
Conjunctivitis			

subjects affected / exposed	4 / 3939 (0.10%)		
occurrences (all)	4		
Tonsillitis			
subjects affected / exposed	6 / 3939 (0.15%)		
occurrences (all)	6		
Upper respiratory tract infection			
subjects affected / exposed	3 / 3939 (0.08%)		
occurrences (all)	3		
Influenza			
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Cellulitis			
subjects affected / exposed	4 / 3939 (0.10%)		
occurrences (all)	4		
Acute sinusitis			
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Herpangina			
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Laryngitis			
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Viral pharyngitis			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	2 / 3939 (0.05%)		
occurrences (all)	2		
Oral herpes			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Periodontitis			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Pharyngitis streptococcal			

subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 3939 (0.03%)		
occurrences (all)	1		
Bronchitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	94 / 3939 (2.39%)		
occurrences (all)	100		
Nasopharyngitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	82 / 3939 (2.08%)		
occurrences (all)	93		
Pharyngitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	40 / 3939 (1.02%)		
occurrences (all)	42		
Gastroenteritis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	30 / 3939 (0.76%)		
occurrences (all)	31		
Bronchiolitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	28 / 3939 (0.71%)		
occurrences (all)	29		
Otitis media-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	22 / 3939 (0.56%)		
occurrences (all)	22		
Pneumonia-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	15 / 3939 (0.38%)		
occurrences (all)	16		
Rhinitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	13 / 3939 (0.33%)		
occurrences (all)	13		
Conjunctivitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	12 / 3939 (0.30%)		
occurrences (all)	12		
Tonsillitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	17 / 3939 (0.43%)		
occurrences (all)	17		
Upper respiratory tract infection-	Additional description: This symptom was assessed as a MAAE.		

MAAE			
subjects affected / exposed	11 / 3939 (0.28%)		
occurrences (all)	11		
Influenza-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	8 / 3939 (0.20%)		
occurrences (all)	8		
Cellulitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	6 / 3939 (0.15%)		
occurrences (all)	6		
Acute sinusitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	5 / 3939 (0.13%)		
occurrences (all)	5		
Impetigo-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	5 / 3939 (0.13%)		
occurrences (all)	5		
Herpes dermatitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	4 / 3939 (0.10%)		
occurrences (all)	4		
Otitis media acute-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	4 / 3939 (0.10%)		
occurrences (all)	4		
Hand-foot-and-mouth disease-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	3 / 3939 (0.08%)		
occurrences (all)	3		
Herpangina-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	3 / 3939 (0.08%)		
occurrences (all)	3		
Laryngitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	3 / 3939 (0.08%)		
occurrences (all)	3		
Oral candidiasis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	3 / 3939 (0.08%)		
occurrences (all)	3		
Viral pharyngitis-MAAE	Additional description: This symptom was assessed as a MAAE.		
subjects affected / exposed	3 / 3939 (0.08%)		
occurrences (all)	3		

Cystitis-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	2 / 3939 (0.05%) 2	
Oral herpes-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	2 / 3939 (0.05%) 2	
Pharyngitis bacterial-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	2 / 3939 (0.05%) 2	
Pharyngotonsillitis-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	2 / 3939 (0.05%) 2	
Tracheitis-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	2 / 3939 (0.05%) 2	
Bacterial infection-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	1 / 3939 (0.03%) 1	
Croup infectious-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	1 / 3939 (0.03%) 1	
Exanthema subitum-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	1 / 3939 (0.03%) 1	
Gastrointestinal infection-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	1 / 3939 (0.03%) 1	
Hordeolum-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	1 / 3939 (0.03%) 1	
Periodontitis-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	1 / 3939 (0.03%) 1	
Pharyngitis streptococcal-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.	
	1 / 3939 (0.03%) 1	

Sinusitis-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.		
	1 / 3939 (0.03%) 1		
Urinary tract infection-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.		
	1 / 3939 (0.03%) 1		
Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all)			
	1 / 3939 (0.03%) 1		
Vitamin D deficiency-MAAE subjects affected / exposed occurrences (all)	Additional description: This symptom was assessed as a MAAE.		
	1 / 3939 (0.03%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 May 2013	Rationale for change: Change in target population from 11-55 years of age to 2-55 years of age. Allow Assent Form provided to minors when requested by IRBs. Change in the solicited local and systemic events description. Exclusion criteria numbered. Change of Korea Food and Drug Administration (KFDA) to Ministry of Food and Drug Safety (MFDS)
22 October 2014	Rationale for change: Change in the location of the injection including infants. Change in the study population, adding infants from 2 to 23 months. Text added to clarify the procedure of infant vaccination. Inclusion of infants in standard temperature measurement. Text included to ensure that infants were not enrolled more than once. Spontaneous reporting applied to this PMS studies. Procedure correction involving the CRO instead of NVD. Clarification that additional SAP will be performed to follow ICH requirements.
12 May 2015	Rationale for change: Text included- For subjects 2-23 months of age, the parents will also be asked to consent for surveillance after subsequent vaccinations. Some texts changed to align with Korean Health Authorities. Study time and events table was modified to include infant subjects. Clarification of study participation duration.
25 August 2015	Rationale for change: Due to change of Marketing Authorization Holder from Novartis Vaccines to GSK Vaccines, the document was revised to change name of Sponsor.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported