Clinical trial results:
A randomised, open-label study to assess the immunogenicity and reactogenicity of GSK Biologicals' IPV vaccine administered as a three-dose primary vaccination course at 2-3-4 months of age in healthy infants in China.

Summary

EudraCT number	2011-003167-30
Trial protocol	Outside EU/EEA
Global end of trial date	05 July 2010

Results information

Result version number	v1
This version publication date	08 April 2016
First version publication date	01 July 2015

Trial information

Trial identification

Sponsor protocol code	112679

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01021293
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	Final
Date of interim/final analysis	05 July 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 July 2010
Global end of trial reached?	Yes
Global end of trial date	05 July 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of GSK Biologicals' IPV vaccine as compared to the Chinese OPV vaccine in terms of the immune response to poliovirus type 1, 2 and 3, one month after the third vaccine dose.
Non-inferiority in terms of immunogenicity to the three poliovirus antigens will be demonstrated if the upper limit of the 95% confidence interval (CI) on the group difference [Control Group minus Poliorix Group] in the percentage of seroprotected subjects is less than or equal to 10%.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 November 2009
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	China: 1101
Worldwide total number of subjects	1101
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)	1101
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Of the 1101 enrolled subjects, one subject was not randomised and administered any vaccine as the parents of the subject refused to vaccinate their child after blood collection at Visit 1 and withdrew their consent.

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 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	IPV Group

Arm description:

Subjects received 3 doses of IPV vaccine at 2, 3 and 4 months of age.

Arm type	Experimental
Investigational medicinal product name	Poliorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of IPV vaccine administered intramuscularly into the anterolateral side of the right thigh

Arm title	Control Group

Arm description:

Subjects received 3 doses of OPV vaccine at 2, 3 and 4 months of age.

Arm type	Active comparator
Investigational medicinal product name	Oral Poliomyelitis Vaccine (OPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

3 doses of OPV vaccine administered orally

Number of subjects in period 1[1]	IPV Group	Control Group
Started	550	550
Completed	538	526
Not completed	12	24
Adverse event, serious fatal	2	1
Consent withdrawn by subject	1	3
Adverse event, non-fatal	2	1
Migrated/moved from study area	6	18
Lost to follow-up	1	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: Of the 1101 enrolled subjects, one subject was not randomised and administered any vaccine as the parents of the subject refused to vaccinate their child after blood collection at Visit 1 and withdrew their consent.

Baseline characteristics

Reporting groups	
Reporting group title	IPV Group
Reporting group description:	
Subjects received 3 doses of IPV vaccine at 2, 3 and 4 months of age.	
Reporting group title	Control Group
Reporting group description:	
Subjects received 3 doses of OPV vaccine at 2, 3 and 4 months of age.	

Reporting group values	IPV Group	Control Group	Total
Number of subjects	550	550	1100
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: weeks			
arithmetic mean	10	10.1	
standard deviation	± 1.16	± 1.18	-
Gender categorical Units: Subjects			
Female	268	259	527
Male	282	291	573

End points

End points reporting groups

Reporting group title	IPV Group
Reporting group description:	
Subjects received 3 doses of IPV vaccine at 2, 3 and 4 months of age.	
Reporting group title	Control Group
Reporting group description:	
Subjects received 3 doses of OPV vaccine at 2, 3 and 4 months of age.	

Primary: Number of seroprotected subjects against anti-poliovirus types 1, 2 and 3

End point title	Number of seroprotected subjects against anti-poliovirus types 1, 2 and 3
End point description:	
End point type	Primary
End point timeframe:	
One month after the third dose of primary vaccination (Month 3).	

End point values	IPV Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	306	296		
Units: Subjects				
Anti-poliovirus 1	306	296		
Anti-poliovirus 2	306	296		
Anti-poliovirus 3	306	291		

Statistical analyses

Statistical analysis title	Non-inferiority of IPV as compared to OPV
Statistical analysis description:	
Non-inferiority of IPV vaccine as compared to OPV vaccine in terms of the immune response to poliovirus type 1 one month after the third vaccine dose. Non-inferiority in terms of immunogenicity to poliovirus antigens was demonstrated if the upper limit of the 95% confidence interval (CI) on the group difference [Control Group minus IPV Group] in the percentage of seroprotected subjects was ≤ 10%.	
Comparison groups	IPV Group v Control Group
Number of subjects included in analysis	602
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in seroprotection rate
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	1.24

Statistical analysis title	Non-inferiority of IPV as compared to OPV

Statistical analysis description:

Non-inferiority of IPV vaccine as compared to OPV vaccine in terms of the immune response to poliovirus type 2 one month after the third vaccine dose. Non-inferiority in terms of immunogenicity to poliovirus antigens was demonstrated if the upper limit of the 95% confidence interval (CI) on the group difference [Control Group minus IPV Group] in the percentage of seroprotected subjects was ≤ 10%.

Comparison groups	IPV Group v Control Group
Number of subjects included in analysis	602
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in seroprotection rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	1.24

Statistical analysis title	Non-inferiority of IPV as compared to OPV

Statistical analysis description:

Non-inferiority of IPV vaccine as compared to OPV vaccine in terms of the immune response to poliovirus type 3 one month after the third vaccine dose. Non-inferiority in terms of immunogenicity to poliovirus antigens was demonstrated if the upper limit of the 95% confidence interval (CI) on the group difference [Control Group minus IPV Group] in the percentage of seroprotected subjects was ≤ 10%.

Comparison groups	IPV Group v Control Group
Number of subjects included in analysis	602
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in seroprotection rate
Point estimate	-1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	-0.44

Secondary: Number of seroprotected subjects against anti-poliovirus types 1, 2 and 3

End point title	Number of seroprotected subjects against anti-poliovirus types 1, 2 and 3

End point description:

A seroprotected subject was defined as a subject whose antibody titre was ≥ 8 ED50.

End point type	Secondary

End point timeframe:

Prior to the first dose of primary vaccination (Day 0)

End point values	IPV Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	306	296		
Units: Subjects				
Anti-poliovirus 1	131	113		
Anti-poliovirus 2	93	99		
Anti-poliovirus 3	48	52		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titres against each of the three poliovirus types

End point title	Antibody titres against each of the three poliovirus types

End point description:

Antibody titers were summarized by geometric mean titers (GMTs) with their 95% CIs. The three virus types were poliovirus types 1, 2 and 3

End point type	Secondary

End point timeframe:

Prior to the first dose and one month after the third dose of primary vaccination (Day 0 and Month 3)

End point values	IPV Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	306	296		
Units: Titre				
geometric mean (confidence interval 95%)				
Anti-poliovirus 1; Day 0	8.7 (7.6 to 9.8)	7.8 (6.9 to 8.9)		
Anti-poliovirus 2; Day 0	6.5 (5.9 to 7.1)	7.2 (6.5 to 8.1)		
Anti-poliovirus 3; Day 0	5.2 (4.8 to 5.7)	5.2 (4.8 to 5.7)		
Anti-poliovirus 1; Month 3	485.1 (436.7 to 538.9)	2817 (2479.5 to 3200.4)		
Anti-poliovirus 2; Month 3	234.3 (209 to 262.6)	468.5 (416.6 to 526.9)		
Anti-poliovirus 3; Month 3	824.3 (725.3 to 936.9)	423.4 (363.3 to 493.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptoms

End point title	Number of subjects reporting any and grade 3 solicited local symptoms[1]

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = Cry when limb is moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site. This outcome measure concerns subjects from the IPV Group only.

End point type	Secondary

End point timeframe:

During the 4-day (Day 0–3) follow-up period following each dose of the study vaccines

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 outcome measure concerns subjects from the IPV Group only.

End point values	IPV Group			
Subject group type	Reporting group			
Number of subjects analysed	550			
Units: Subjects				
Any Pain; Dose 1	80			
Grade 3 Pain; Dose 1	1			
Any Redness; Dose 1	20			
Grade 3 Redness; Dose 1	0			
Any Swelling; Dose 1	9			
Grade 3 Swelling; Dose 1	0			
Any Pain; Dose 2	58			
Grade 3 Pain; Dose 2	2			
Any Redness; Dose 2	23			
Grade 3 Redness; Dose 2	1			
Any Swelling; Dose 2	8			
Grade 3 Swelling; Dose 2	1			
Any Pain; Dose 3	41			
Grade 3 Pain; Dose 3	0			
Any Redness; Dose 3	15			
Grade 3 Redness; Dose 3	0			
Any Swelling; Dose 3	6			
Grade 3 Swelling; Dose 3	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms

End point title	Number of subjects reporting any, grade 3 and related solicited general symptoms

End point description:

Assessed solicited general symptoms were drowsiness, gastrointestinal symptoms, irritability/fussiness, loss of appetite and fever. Gastrointestinal symptoms included nausea, vomiting, diarrhoea and/or abdominal pain. Any = occurrence of the symptom regardless of intensity grade. Grade 3 drowsiness = drowsiness that prevented normal activity, Grade 3 irritability = crying that could not be comforted/ prevented normal activity, Grade 3 loss of appetite = subject did not eat at all, Grade 3 gastrointestinal symptoms = gastrointestinal symptoms that prevented normal activity. Related = symptom assessed by the investigator as causally related to the vaccination.

End point type	Secondary

End point timeframe:

During the 4-day (Day 0–3) follow-up period following each dose of the study vaccines

End point values	IPV Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	550		
Units: Subjects				
Any Drowsiness; Dose 1	99	75		
Grade 3 Drowsiness; Dose 1	0	1		
Related Drowsiness; Dose 1	71	51		
Any Gastrointestinal Symptoms; Dose 1	102	89		
Grade 3 Gastrointestinal Symptoms, Dose 1	0	2		
Related Gastrointestinal Symptoms; Dose 1	44	43		
Any Irritability/Fussiness; Dose 1	160	151		
Grade 3 Irritability/Fussiness; Dose 1	1	5		
Related Irritability/Fussiness; Dose 1	130	105		
Any Loss of appetite; Dose 1	82	83		
Grade 3 Loss of appetite; Dose 1	0	1		
Related Loss of appetite; Dose 1	54	47		
Any temperature; Dose 1	39	20		
Grade 3 temperature; Dose 1	0	0		
Related temperature; Dose 1	28	10		
Any Drowsiness; Dose 2	68	50		
Grade 3 Drowsiness; Dose 2	2	0		
Related Drowsiness; Dose 2	51	25		
Any Gastrointestinal Symptoms; Dose 2	66	67		
Grade 3 Gastrointestinal Symptoms, Dose 2	2	1		
Related Gastrointestinal Symptoms; Dose 2	32	35		
Any Irritability/Fussiness; Dose 2	121	86		
Grade 3 Irritability/Fussiness; Dose 2	7	2		
Related Irritability/Fussiness; Dose 2	105	50		

Any Loss of appetite; Dose 2	70	78		
Grade 3 Loss of appetite; Dose 2	3	0		
Related Loss of appetite; Dose 2	48	47		
Any temperature; Dose 2	39	26		
Grade 3 temperature; Dose 2	2	1		
Related temperature; Dose 2	29	11		
Any Drowsiness; Dose 3	47	45		
Grade 3 Drowsiness; Dose 3	2	1		
Related Drowsiness; Dose 3	36	25		
Any Gastrointestinal Symptoms; Dose 3	46	67		
Grade 3 Gastrointestinal Symptoms, Dose 3	3	0		
Related Gastrointestinal Symptoms; Dose 3	16	25		
Any Irritability/Fussiness; Dose 3	87	72		
Grade 3 Irritability/Fussiness; Dose 3	2	2		
Related Irritability/Fussiness; Dose 3	77	44		
Any Loss of appetite; Dose 3	52	64		
Grade 3 Loss of appetite; Dose 3	0	0		
Related Loss of appetite; Dose 3	34	36		
Any temperature; Dose 3	33	32		
Grade 3 temperature; Dose 3	0	2		
Related temperature; Dose 3	18	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse event

End point title	Number of subjects reporting any unsolicited adverse event

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. Any was defined as an adverse event (AE) reported in addition to those solicited during the clinical study. Also any solicited symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.

End point type	Secondary

End point timeframe:

Within the 31-day follow-up period following each dose of the study vaccines

End point values	IPV Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	550		
Units: Subjects				
Any AE(s)	155	162		

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:

Serious adverse events (SAEs) assessed include medical occurrences that results in death, are life threatening, requires hospitalization or prolongation of hospitalization or results in disability/incapacity.

End point type	Secondary

End point timeframe:

During the entire study period (Day 0 to Month 3)

End point values	IPV Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	550	550		
Units: Subjects				
Any SAE(s)	3	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local & general symptoms were collected during the 4-day post-vaccination period. Unsolicited AEs were collected within the 31-day follow-up period after each vaccine dose.SAEs were collected during the entire study period (Day 0 - Month 3)

Adverse event reporting additional description:

The number of occurrences reported for serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	IPV Group

Reporting group description:

Subjects received 3 doses of IPV vaccine at 2, 3 and 4 months of age.

Reporting group title	Control Group

Reporting group description:

Subjects received 3 doses of OPV vaccine at 2, 3 and 4 months of age.

Serious adverse events	IPV Group	Control Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 550 (0.55%)	6 / 550 (1.09%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Cardiac disorders			
Cardiac failure			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 550 (0.00%)	1 / 550 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 550 (0.00%)	1 / 550 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
alternative assessment type: Non-			

systematic			
subjects affected / exposed	1 / 550 (0.18%)	0 / 550 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 550 (0.00%)	1 / 550 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 550 (0.18%)	0 / 550 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 550 (0.00%)	1 / 550 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 550 (0.00%)	1 / 550 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchopneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 550 (0.00%)	2 / 550 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
alternative assessment type: Non-			

systematic			
subjects affected / exposed	0 / 550 (0.00%)	1 / 550 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 550 (0.18%)	0 / 550 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 550 (0.00%)	1 / 550 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	IPV Group	Control Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	160 / 550 (29.09%)	151 / 550 (27.45%)	
General disorders and administration site conditions			
Pain; Dose 1			
subjects affected / exposed	80 / 550 (14.55%)	0 / 550 (0.00%)	
occurrences (all)	80	0	
Pain; Dose 2			
subjects affected / exposed[1]	58 / 543 (10.68%)	0 / 543 (0.00%)	
occurrences (all)	58	0	
Pain; Dose 3			
subjects affected / exposed[2]	41 / 540 (7.59%)	0 / 540 (0.00%)	
occurrences (all)	41	0	
Drowsiness; Dose 1			
subjects affected / exposed	99 / 550 (18.00%)	75 / 550 (13.64%)	
occurrences (all)	99	75	
Gastrointestinal Symptoms; Dose 1			

subjects affected / exposed	102 / 550 (18.55%)	89 / 550 (16.18%)	
occurrences (all)	102	89	
Irritability/Fussiness; Dose 1			
subjects affected / exposed	160 / 550 (29.09%)	151 / 550 (27.45%)	
occurrences (all)	160	151	
Loss of appetite; Dose 1			
subjects affected / exposed	82 / 550 (14.91%)	83 / 550 (15.09%)	
occurrences (all)	82	83	
Fever; Dose 1			
subjects affected / exposed	39 / 550 (7.09%)	20 / 550 (3.64%)	
occurrences (all)	39	20	
Drowsiness; Dose 2			
subjects affected / exposed[3]	68 / 543 (12.52%)	50 / 544 (9.19%)	
occurrences (all)	68	50	
Gastrointestinal Symptoms; Dose 2			
subjects affected / exposed[4]	66 / 543 (12.15%)	67 / 544 (12.32%)	
occurrences (all)	66	67	
Irritability/Fussiness; Dose 2			
subjects affected / exposed[5]	121 / 543 (22.28%)	86 / 544 (15.81%)	
occurrences (all)	121	86	
Loss of appetite; Dose 2			
subjects affected / exposed[6]	70 / 543 (12.89%)	78 / 544 (14.34%)	
occurrences (all)	70	78	
Fever; Dose 2			
subjects affected / exposed[7]	39 / 543 (7.18%)	26 / 544 (4.78%)	
occurrences (all)	39	26	
Drowsiness; Dose 3			
subjects affected / exposed[8]	47 / 540 (8.70%)	45 / 534 (8.43%)	
occurrences (all)	47	45	
Gastrointestinal Symptoms; Dose 3			
subjects affected / exposed[9]	46 / 540 (8.52%)	67 / 534 (12.55%)	
occurrences (all)	46	67	
Irritability/Fussiness; Dose 3			
subjects affected / exposed[10]	87 / 540 (16.11%)	72 / 534 (13.48%)	
occurrences (all)	87	72	
Loss of appetite; Dose 3			

subjects affected / exposed[11]	52 / 540 (9.63%)	64 / 534 (11.99%)	
occurrences (all)	52	64	
Fever; Dose 3			
subjects affected / exposed[12]	33 / 540 (6.11%)	32 / 534 (5.99%)	
occurrences (all)	33	32	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	99 / 550 (18.00%)	97 / 550 (17.64%)	
occurrences (all)	99	97	
Nasopharyngitis			
subjects affected / exposed	32 / 550 (5.82%)	38 / 550 (6.91%)	
occurrences (all)	32	38	

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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen 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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen 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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen 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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen 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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen 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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen 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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen completed).
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen completed).
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects

exposed for the reporting group. These numbers are expected to be equal.

Justification: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen completed).

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

Justification: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen completed).

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

Justification: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen completed).

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

Justification: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen 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