Clinical trial results:
A phase IIIA, randomized, observer-blind, controlled, multinational study to evaluate the immunogenicity and safety of GSK Biologicals' MMR vaccine (209762) (Priorix) at an end of shelf-life potency compared to Merck & Co., Inc.’s MMR vaccine (M-M-R II), when both are co-administered with Varivax, Havrix and Prevnar 13 (subset of children), and given on a two-dose schedule to healthy children in their second year of life

Summary

EudraCT number	2011-004905-26
Trial protocol	FI CZ ES
Global end of trial date	18 August 2015

Results information

Result version number	v2 (current)
This version publication date	04 August 2018
First version publication date	15 January 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	115649

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01681992
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 Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, 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	14 September 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To demonstrate non-inferiority of Inv_MMR_Min vaccine compared to pooled Com_MMR vaccine in terms of seroresponse rates & GMCs for antibodies to MMR viruses at Day 42. 2. To demonstrate an acceptable immune response of Inv_MMR_Min & Inv_MMR_Med vaccine in terms of seroresponse rates for MMR viruses at Day 42. 3. To demonstrate non-inferiority of Inv_MMR_Min vaccine compared to pooled Com_MMR vaccine in terms of seroresponse rates & GMTs for antibodies to mumps virus (by PRNT) at Day 42. 4. To demonstrate non-inferiority of Inv_MMR_Med vaccine compared to pooled Com_MMR vaccine in terms of seroresponse rates & GMCs for antibodies to MMR viruses at Day 42. 5. To demonstrate non-inferiority of Inv_MMR_Med vaccine compared to pooled Com_MMR vaccine in terms of seroresponse rates & GMTs for antibodies to mumps virus (by PRNT) at Day 42.

Protection of trial subjects:

All subjects were observed closely for at least 30 minutes following the administration of vaccines with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 October 2012
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	Czech Republic: 700
Country: Number of subjects enrolled	Finland: 421
Country: Number of subjects enrolled	Malaysia: 134
Country: Number of subjects enrolled	Spain: 1300
Country: Number of subjects enrolled	Thailand: 966
Country: Number of subjects enrolled	United States: 1017
Worldwide total number of subjects	4538
EEA total number of subjects	2421

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)	4538
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:

US sub-cohort: Subjects recruited in US and received Inv_MMR_Min or Inv_MMR_Med or Com_MMR (Lot 1 or 2) co-administered with Varivax (VV), Havrix (HAV) and Prevnar 13 (PCV-13) at Day 0. Non-US sub-cohort: Subjects recruited outside US and received Inv_MMR_Min or Inv_MMR_Med or Com_MMR (Lot 1 or 2) co-administered with VV and HAV at Day 0.

Pre-assignment

Screening details:

4538 subjects were registered in the study. 3 subjects were excluded because of invalid Informed Consent Forms and 19 subjects received a subject number but were not vaccinated. Therefore, the number of subjects started is 4516.

Pre-assignment period milestones

Number of subjects started	4538
Number of subjects completed	4516

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Subject number allocated but not vaccinated: 19
Reason: Number of subjects	Invalid Informed Consent Forms: 3

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind[1]
Roles blinded	Subject, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The study was conducted in a double-blind fashion with regard to the two Inv_MMR vaccine lots (Inv_MMR_Min and Inv_MMR_Med) and in an observer-blind fashion for the lots of Inv_MMR vaccine versus the pooled Com_MMR vaccine lots. By observer-blind, it is meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint were all unaware of which vaccine was administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	Inv_MMR_Min Group

Arm description:

Subjects received one dose of GlaxoSmithKline (GSK) Biologicals' measles, mumps, rubella (MMR) vaccine, Priorix (Inv_MMR), from a minimum potency lot (Inv_MMR_Min), co-administered with Varivax (VV) and Havrix (HAV) vaccines at Day 0. All US subjects were also co-administered Prevnar 13 (PCV-13) vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose from a separate lot of the Inv_MMR vaccine (Inv_MMR_Release), for the second dose. Inv_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Arm type	Experimental
Investigational medicinal product name	Priorix
Investigational medicinal product code	
Other name	GSK Biologicals' live attenuated measles, mumps, rubella vaccine
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received one dose of either minimum (Inv_MMR_Min) or medium (Inv_MMR_Med) potency lot at Day 0 and a dose of separate potency lot (Inv_MMR_Release) at Day 42, administered subcutaneously in the triceps region of the left arm.

Investigational medicinal product name	Varivax
Investigational medicinal product code	
Other name	Merck & Co., Inc.’s varicella virus vaccine, live
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received one dose co-administered subcutaneously with the study vaccines (Priorix and M-M-R II), in the triceps region of right arm, at Day 0.

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	GSK Biologicals’ hepatitis A vaccine, inactivated
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received one dose co-administered intramuscularly with the study vaccines (Priorix and M-M-R II), in the anterolateral region of the right thigh, at Day 0.

Investigational medicinal product name	Prevnar 13
Investigational medicinal product code	
Other name	Pfizer Inc.’s pneumococcal 13-valent conjugate vaccine (diphtheria CRM197 protein)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

US Subjects received one dose co-administered intramuscularly with the study vaccines (Priorix and M-M-R II), in the anterolateral region of the left thigh, at Day 0.

Arm title	Inv_MMR_Med Group

Arm description:

Subjects received one dose of GlaxoSmithKline (GSK) Biologicals’ measles, mumps, rubella (MMR) vaccine, Priorix (Inv_MMR), from a mid-range or medium potency lot (Inv_MMR_Med), co-administered with Varivax (VV) and Havrix (HAV) vaccines at Day 0. All US subjects were also co-administered Prevnar 13 (PCV-13) vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose from a separate lot of the Inv_MMR vaccine (Inv_MMR_Release), for the second dose. Inv_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Arm type	Experimental
Investigational medicinal product name	Priorix
Investigational medicinal product code	
Other name	GSK Biologicals’ live attenuated measles, mumps, rubella vaccine
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received one dose of either minimum (Inv_MMR_Min) or medium (Inv_MMR_Med) potency lot at Day 0 and a dose of separate potency lot (Inv_MMR_Release) at Day 42, administered subcutaneously in the triceps region of the left arm.

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	GSK Biologicals’ hepatitis A vaccine, inactivated
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received one dose co-administered intramuscularly with the study vaccines (Priorix and M-M-R II), in the anterolateral region of the right thigh, at Day 0.

Investigational medicinal product name	Prevnar 13
Investigational medicinal product code	
Other name	Pfizer Inc.’s pneumococcal 13-valent conjugate vaccine (diphtheria CRM197 protein)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

US Subjects received one dose co-administered intramuscularly with the study vaccines (Priorix and M-M-R II), in the anterolateral region of the left thigh, at Day 0.

Investigational medicinal product name	Varivax
Investigational medicinal product code	
Other name	Merck & Co., Inc.’s varicella virus vaccine, live
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received one dose co-administered subcutaneously with the study vaccines (Priorix and M-M-R II), in the triceps region of right arm, at Day 0.

Arm title	Com_MMR Group

Arm description:

Subjects received one dose of M-M-R II (Com_MMR) vaccine (Lot 1 or Lot 2), co-administered with Varivax (VV) and Havrix (HAV) vaccines at Day 0. All US subjects were also co-administered Prevnar 13 (PCV-13) vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose of Com_MMR vaccine (Lot 1 or Lot 2), for the second dose. Com_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Arm type	Active comparator
Investigational medicinal product name	M-M-R II
Investigational medicinal product code	
Other name	Merck & Co., Inc.’s measles, mumps, rubella virus vaccine, live
Pharmaceutical forms	Powder and solvent for suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received two doses of either Lot 1 or Lot 2, one at Day 0 and one at Day 42, administered subcutaneously in the triceps region of the left arm.

Investigational medicinal product name	Varivax
Investigational medicinal product code	
Other name	Merck & Co., Inc.’s varicella virus vaccine, live
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received one dose co-administered subcutaneously with the study vaccines (Priorix and M-M-R II), in the triceps region of right arm, at Day 0.

Investigational medicinal product name	Havrix
Investigational medicinal product code	
Other name	GSK Biologicals’ hepatitis A vaccine, inactivated
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received one dose co-administered intramuscularly with the study vaccines (Priorix and M-M-R II), in the anterolateral region of the right thigh, at Day 0.

Investigational medicinal product name	Prevnar 13
Investigational medicinal product code	
Other name	Pfizer Inc.’s pneumococcal 13-valent conjugate vaccine (diphtheria CRM197 protein)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

US Subjects received one dose co-administered intramuscularly with the study vaccines (Priorix and M-M-R II), in the anterolateral region of the left thigh, at Day 0.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: The study was conducted in a double-blind fashion with regard to the two Inv_MMR vaccine lots (Inv_MMR_Min and Inv_MMR_Med) and in an observer-blind fashion for the lots of Inv_MMR vaccine versus the pooled Com_MMR vaccine lots.

Number of subjects in period 1[2]	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group
Started	1493	1497	1526
Completed	1427	1427	1443
Not completed	66	70	83
Consent withdrawn by subject	27	30	25
Adverse event, non-fatal	3	2	3
As Per Sponsor Decision	-	-	1
Lost to follow-up	36	38	53
Protocol deviation	-	-	1

Notes:

[2] - 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: 4538 subjects were registered in the study. 3 subjects were excluded because of invalid Informed Consent Forms and 19 subjects received a subject number but were not vaccinated. Therefore, the number of subjects started is 4516.

Baseline characteristics

Reporting groups	
Reporting group title	Inv_MMR_Min Group
Reporting group description:	
Subjects received one dose of GlaxoSmithKline (GSK) Biologicals' measles, mumps, rubella (MMR) vaccine, Priorix (Inv_MMR), from a minimum potency lot (Inv_MMR_Min), co-administered with Varivax (VV) and Havrix (HAV) vaccines at Day 0. All US subjects were also co-administered Prevnar 13 (PCV-13) vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose from a separate lot of the Inv_MMR vaccine (Inv_MMR_Release), for the second dose. Inv_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.	
Reporting group title	Inv_MMR_Med Group
Reporting group description:	
Subjects received one dose of GlaxoSmithKline (GSK) Biologicals' measles, mumps, rubella (MMR) vaccine, Priorix (Inv_MMR), from a mid-range or medium potency lot (Inv_MMR_Med), co-administered with Varivax (VV) and Havrix (HAV) vaccines at Day 0. All US subjects were also co-administered Prevnar 13 (PCV-13) vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose from a separate lot of the Inv_MMR vaccine (Inv_MMR_Release), for the second dose. Inv_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.	
Reporting group title	Com_MMR Group
Reporting group description:	
Subjects received one dose of M-M-R II (Com_MMR) vaccine (Lot 1 or Lot 2), co-administered with Varivax (VV) and Havrix (HAV) vaccines at Day 0. All US subjects were also co-administered Prevnar 13 (PCV-13) vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose of Com_MMR vaccine (Lot 1 or Lot 2), for the second dose. Com_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.	

Reporting group values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group
Number of subjects	1493	1497	1526
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	12.6	12.6	12.6
standard deviation	± 0.9	± 0.9	± 0.9
Gender categorical Units: Subjects			
Female	704	718	758
Male	789	779	768
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American	45	53	46
American Indian or Alaskan Native	2	1	1
Asian - Central/South Asian Heritage	1	0	2
Asian - East Asian Heritage	3	0	1
Asian - South East Asian Heritage	362	366	367

Native Hawaiian or Other Pacific Islander	0	1	0
White - Arabic / North African Heritage	8	8	8
White - Caucasian / European Heritage	1017	1022	1052
Other	55	46	49

Reporting group values	Total		
Number of subjects	4516		
Age categorical Units: Subjects			

Age continuous Units: months			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	2180		
Male	2336		
Race/Ethnicity, Customized Units: Subjects			
African Heritage / African American	144		
American Indian or Alaskan Native	4		
Asian - Central/South Asian Heritage	3		
Asian - East Asian Heritage	4		
Asian - South East Asian Heritage	1095		
Native Hawaiian or Other Pacific Islander	1		
White - Arabic / North African Heritage	24		
White - Caucasian / European Heritage	3091		
Other	150		

End points

End points reporting groups

Reporting group title	Inv_MMR_Min Group

Reporting group description:

Subjects received one dose of GlaxoSmithKline (GSK) Biologicals' measles, mumps, rubella (MMR) vaccine, Priorix (Inv_MMR), from a minimum potency lot (Inv_MMR_Min), co-administered with Varivax (VV) and Havrix (HAV) vaccines at Day 0. All US subjects were also co-administered Prevnar 13 (PCV-13) vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose from a separate lot of the Inv_MMR vaccine (Inv_MMR_Release), for the second dose. Inv_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Reporting group title	Inv_MMR_Med Group

Reporting group description:

Subjects received one dose of GlaxoSmithKline (GSK) Biologicals' measles, mumps, rubella (MMR) vaccine, Priorix (Inv_MMR), from a mid-range or medium potency lot (Inv_MMR_Med), co-administered with Varivax (VV) and Havrix (HAV) vaccines at Day 0. All US subjects were also co-administered Prevnar 13 (PCV-13) vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose from a separate lot of the Inv_MMR vaccine (Inv_MMR_Release), for the second dose. Inv_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Reporting group title	Com_MMR Group

Reporting group description:

Subjects received one dose of M-M-R II (Com_MMR) vaccine (Lot 1 or Lot 2), co-administered with Varivax (VV) and Havrix (HAV) vaccines at Day 0. All US subjects were also co-administered Prevnar 13 (PCV-13) vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose of Com_MMR vaccine (Lot 1 or Lot 2), for the second dose. Com_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Primary: Percentage of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value (by enzyme-linked immunosorbent assay [ELISA])

End point title	Percentage of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value (by enzyme-linked immunosorbent assay [ELISA])

End point description:

For measles virus, a seroresponse was defined as post-vaccination anti-measles virus antibody concentration equal or above [≥] 200 mIU/mL (ELISA) among subjects who were seronegative (antibody concentration less than [<] 150 mIU/mL) before dose 1. Criteria to demonstrate an acceptable immune response of Inv_MMR_Min/Inv_MMR_Med vaccine in terms of seroresponse rate for measles virus at Day 42: The lower limit of the two-sided 97.5% CI for the seroresponse rate of Inv_MMR_Min/Inv_MMR_Med was to be ≥ 90% for antibodies to measles virus.

End point type	Primary

End point timeframe:

At Day 42

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1361	1366	1378	
Units: Percentage of subjects				
number (confidence interval 97.5%)				
Anti-measles ≥ 150 mIU/mL	90.9 (89.0 to 92.6)	94.3 (92.7 to 95.6)	96.5 (95.2 to 97.5)	
Anti-measles ≥ 200 mIU/mL	90.8 (88.9 to 92.5)	94.2 (92.6 to 95.5)	96.3 (95.0 to 97.3)	

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Non-inferiority of Inv_MMR_Min vaccine compared to Com_MMR vaccine in terms of seroresponse rate to measles virus at Day 42.

Comparison groups	Inv_MMR_Min Group v Com_MMR Group
Number of subjects included in analysis	2739
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in seroresponse rate
Point estimate	-5.48
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-7.65
upper limit	-3.43

Notes:

[1] - The lower limit of the 2-sided 97.5% confidence interval (CI) on the group difference (Inv_MMR_Min minus Com_MMR) in seroresponse rate should be ≥ -5% for antibodies to measles virus when tested with ELISA.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Non-inferiority of Inv_MMR_Med vaccine compared to Com_MMR vaccine in terms of seroresponse rate to measles virus at Day 42.

Comparison groups	Com_MMR Group v Inv_MMR_Med Group
Number of subjects included in analysis	2744
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in seroresponse rate
Point estimate	-2.08
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-3.96
upper limit	-0.27

Notes:

[2] - The lower limit of the 2-sided 97.5% confidence interval (CI) on the group difference (Inv_MMR_Med minus Com_MMR) in seroresponse rate should be ≥ -5% for antibodies to measles virus when tested with ELISA.

Primary: Percentage of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value (by ELISA)

End point title	Percentage of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value (by ELISA)

End point description:

For mumps virus, a seroresponse was defined as post-vaccination anti-mumps virus antibody concentration ≥ 10 EU/mL (ELISA) among subjects who were seronegative (antibody concentration < 5 EU/mL) before dose 1. Criteria to demonstrate an acceptable immune response of Inv_MMR_Min/Inv_MMR_Med vaccine in terms of seroresponse rate for mumps virus at Day 42: The lower limit of the two-sided 97.5% CI for the seroresponse rate of Inv_MMR_Min/Inv_MMR_Med was to be ≥ 90% for antibodies to mumps virus.

End point type	Primary

End point timeframe:

At Day 42

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1161	1131	1155	
Units: Percentage of subjects				
number (confidence interval 97.5%)				
Anti-mumps ≥ 5 EU/mL	99.1 (98.2 to 99.6)	99.0 (98.1 to 99.6)	99.2 (98.4 to 99.7)	
Anti-mumps ≥ 10 EU/mL	97.4 (96.2 to 98.3)	97.3 (96.0 to 98.2)	97.8 (96.7 to 98.7)	

Statistical analyses

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Non-inferiority of Inv_MMR_Med vaccine compared to Com_MMR vaccine in terms of seroresponse rate to mumps virus at Day 42.

Comparison groups	Com_MMR Group v Inv_MMR_Med Group
Number of subjects included in analysis	2286
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in seroresponse rate
Point estimate	-0.58
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.11
upper limit	0.91

Notes:

[3] - The lower limit of the 2-sided 97.5% CI on the group difference (Inv_MMR_Med minus Com_MMR) in seroresponse rate should be ≥ -5% for antibodies to mumps virus when tested with ELISA.

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Non-inferiority of Inv_MMR_Min vaccine compared to Com_MMR vaccine in terms of seroresponse rate

to mumps virus at Day 42.

Comparison groups	Com_MMR Group v Inv_MMR_Min Group
Number of subjects included in analysis	2316
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in seroresponse rate
Point estimate	-0.42
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.91
upper limit	1.04

Notes:

[4] - The lower limit of the 2-sided 97.5% CI on the group difference (Inv_MMR_Min minus Com_MMR) in seroresponse rate should be ≥ -5% for antibodies to mumps virus when tested with ELISA.

Primary: Percentage of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value (by Plaque Reduction Neutralization Test [PRNT])

End point title	Percentage of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value (by Plaque Reduction Neutralization Test [PRNT])

End point description:

For mumps virus as measured by PRNT, a seroresponse was defined as post-vaccination anti-mumps virus antibody concentration ≥ 4 End point Dilution 50% (ED50) (PRNT) among subjects who were seronegative (antibody concentration < 2.5 ED50) before dose 1.

End point type	Primary

End point timeframe:

At Day 42

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1252	1265	1287	
Units: Percentage of subjects				
number (confidence interval 95%)				
≥ 2.5 ED50	79.1 (76.7 to 81.3)	81.6 (79.3 to 83.7)	87.5 (85.6 to 89.2)	
≥ 4 ED50	71.2 (68.6 to 73.7)	73.4 (70.8 to 75.8)	80.6 (78.3 to 82.7)	

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Non-inferiority of Inv_MMR_Min vaccine compared to Com_MMR vaccine in terms of seroresponse rate to mumps virus at Day 42.

Comparison groups	Inv_MMR_Min Group v Com_MMR Group

Number of subjects included in analysis	2539
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Difference in seroresponse rate
Point estimate	-9.41
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-13.2
upper limit	-5.62

Notes:

[5] - The lower limit of the 2-sided 97.5% CI on the group difference (Inv_MMR_Min minus Com_MMR) in seroresponse rate should be ≥ -10% for antibodies to mumps virus when tested with PRNT.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Non-inferiority of Inv_MMR_Med vaccine compared to Com_MMR vaccine in terms of seroresponse rate to mumps virus at Day 42.

Comparison groups	Inv_MMR_Med Group v Com_MMR Group
Number of subjects included in analysis	2552
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Difference in seroresponse rate
Point estimate	-7.22
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-10.94
upper limit	-3.49

Notes:

[6] - The lower limit of the 2-sided 97.5% CI on the group difference (Inv_MMR_Med minus Com_MMR) in seroresponse rate should be ≥ -10% for antibodies to mumps virus when tested with PRNT.

Primary: Percentage of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value (by ELISA)

End point title	Percentage of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value (by ELISA)

End point description:

For rubella virus, a seroresponse was defined as post-vaccination anti-rubella virus antibody concentration ≥ 10 IU/mL (ELISA) among subjects who were seronegative (antibody concentration < 4 IU/mL) before dose 1. Criteria to demonstrate an acceptable immune response of Inv_MMR_Min/Inv_MMR_Med vaccine in terms of seroresponse rate for rubella virus at Day 42: The lower limit of the two-sided 97.5% CI for the seroresponse rate of Inv_MMR_Min/Inv_MMR_Med was to be ≥ 90% for antibodies to mumps virus.

End point type	Primary

End point timeframe:

At Day 42

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1359	1366	1376	
Units: Percentage of subjects				
number (confidence interval 97.5%)				
≥ 4 IU/mL	99.3 (98.6 to 99.7)	99.5 (98.9 to 99.8)	99.5 (98.9 to 99.8)	
≥ 10 IU/mL	96.8 (95.5 to 97.7)	97.3 (96.1 to 98.2)	98.5 (97.6 to 99.1)	

Statistical analyses

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Non-inferiority of Inv_MMR_Med vaccine compared to Com_MMR vaccine in terms of seroresponse rate to rubella virus at Day 42.	
Comparison groups	Com_MMR Group v Inv_MMR_Med Group
Number of subjects included in analysis	2742
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Difference in seroresponse rate
Point estimate	-1.18
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.5
upper limit	0.05

Notes:

[7] - The lower limit of the 2-sided 97.5% CI on the group difference (Inv_MMR_Med minus Com_MMR) in seroresponse rate should be ≥ -5% for antibodies to rubella virus when tested with ELISA.

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Non-inferiority of Inv_MMR_Min vaccine compared to Com_MMR vaccine in terms of seroresponse rate to rubella virus at Day 42.	
Comparison groups	Com_MMR Group v Inv_MMR_Min Group
Number of subjects included in analysis	2735
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Difference in seroresponse rate
Point estimate	-1.71
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-3.11
upper limit	-0.42

Notes:

[8] - The lower limit of the 2-sided 97.5% CI on the group difference (Inv_MMR_Min minus Com_MMR) in seroresponse rate should be ≥ -5% for antibodies to rubella virus when tested with ELISA.

Primary: Anti-measles virus antibody concentrations (by ELISA)

End point title	Anti-measles virus antibody concentrations (by ELISA)
End point description:	
Antibody concentrations were expressed as Geometric Mean Concentrations (GMCs) in mIU/mL.	
End point type	Primary
End point timeframe:	
At Day 42	

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1361	1366	1378	
Units: mIU/mL				
geometric mean (confidence interval 97.5%)				
mIU/mL	2209.9 (2041.3 to 2392.4)	2540.9 (2368.8 to 2725.5)	2787.7 (2619.5 to 2966.7)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Non-inferiority of Inv_MMR_Min vaccine compared to COM_MMR vaccine in terms of GMCs for anti-measles antibodies at Day 42.	
Comparison groups	Com_MMR Group v Inv_MMR_Min Group
Number of subjects included in analysis	2739
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Method	ANOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.79
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.72
upper limit	0.88

Notes:

[9] - The lower limit of the 2-sided 97.5% CI on the group ratio of GMCs (Inv_MMR_Min over pooled Com_MMR) should to be ≥ 0.67 for antibodies to measles virus when tested with ELISA.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Non-inferiority of Inv_MMR_Med vaccine compared to COM_MMR vaccine in terms of GMCs for anti-measles antibodies at Day 42.	
Comparison groups	Inv_MMR_Med Group v Com_MMR Group

Number of subjects included in analysis	2744
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Method	ANOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.91
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.83
upper limit	1.01

Notes:

[10] - The lower limit of the 2-sided 97.5% CI on the group ratio of GMCs (Inv_MMR_Med over pooled Com_MMR) should to be ≥ 0.67 for antibodies to measles virus when tested with ELISA.

Primary: Anti-mumps virus antibody concentrations (by ELISA)

End point title	Anti-mumps virus antibody concentrations (by ELISA)

End point description:

Antibody concentrations were expressed as GMCs in EU/mL.

End point type	Primary

End point timeframe:

At Day 42

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1161	1131	1155	
Units: EU/mL				
geometric mean (confidence interval 97.5%)				
EU/mL	58.7 (55.5 to 62.1)	60.2 (56.8 to 63.7)	71.6 (67.7 to 75.8)	

Statistical analyses

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Non-inferiority of Inv_MMR_Med vaccine compared to COM_MMR vaccine in terms of GMCs for anti-mumps antibodies at Day 42.

Comparison groups	Inv_MMR_Med Group v Com_MMR Group
Number of subjects included in analysis	2286
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Method	ANOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.84

Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.78
upper limit	0.91

Notes:

[11] - The lower limit of the 2-sided 97.5% CI on the group ratio of GMCs (Inv_MMR_Med over pooled Com_MMR) should to be ≥ 0.67 for antibodies to mumps virus when tested with ELISA.

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Non-inferiority of Inv_MMR_Min vaccine compared to COM_MMR vaccine in terms of GMCs for anti-mumps antibodies at Day 42.

Comparison groups	Inv_MMR_Min Group v Com_MMR Group
Number of subjects included in analysis	2316
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Method	ANOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.82
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.76
upper limit	0.89

Notes:

[12] - The lower limit of the 2-sided 97.5% CI on the group ratio of GMCs (Inv_MMR_Min over pooled Com_MMR) should to be ≥ 0.67 for antibodies to mumps virus when tested with ELISA.

Primary: Anti-mumps virus antibody concentrations (by PRNT)

End point title	Anti-mumps virus antibody concentrations (by PRNT)

End point description:

Antibody concentrations were expressed as Geometric Mean Titers (GMTs).

End point type	Primary

End point timeframe:

At Day 42

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1252	1265	1287	
Units: Titers				
geometric mean (confidence interval 95%)				
Titers	9.8 (9.0 to 10.6)	10.7 (9.9 to 11.5)	16.3 (15.1 to 17.7)	

Statistical analyses

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Non-inferiority of Inv_MMR_Med vaccine compared to COM_MMR vaccine in terms of GMCs for anti-mumps antibodies at Day 42.

Comparison groups	Inv_MMR_Med Group v Com_MMR Group
Number of subjects included in analysis	2552
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Method	ANOVA
Parameter estimate	Adjusted GMT ratio
Point estimate	0.65
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.57
upper limit	0.74

Notes:

[13] - The lower limit of the 2-sided 97.5% CI on the group ratio of GMCs (Inv_MMR_Med over pooled Com_MMR) should to be ≥ 0.67 for antibodies to mumps virus when tested with PRNT.

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Non-inferiority of Inv_MMR_Min vaccine compared to COM_MMR vaccine in terms of GMCs for anti-mumps antibodies at Day 42.

Comparison groups	Inv_MMR_Min Group v Com_MMR Group
Number of subjects included in analysis	2539
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Method	ANOVA
Parameter estimate	Adjusted GMT ratio
Point estimate	0.6
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.53
upper limit	0.68

Notes:

[14] - The lower limit of the 2-sided 97.5% CI on the group ratio of GMCs (Inv_MMR_Min over pooled Com_MMR) should to be ≥ 0.67 for antibodies to mumps virus when tested with PRNT.

Primary: Anti-rubella virus antibody concentrations (by ELISA)

End point title	Anti-rubella virus antibody concentrations (by ELISA)

End point description:

Antibody concentrations were expressed as GMCs in IU/mL.

End point type	Primary

End point timeframe:

At Day 42

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1359	1366	1376	
Units: IU/mL				
geometric mean (confidence interval 97.5%)				
IU/mL	57.0 (54.1 to 60.0)	56.9 (54.2 to 59.8)	64.4 (61.4 to 67.5)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Non-inferiority of Inv_MMR_Min vaccine compared to COM_MMR vaccine in terms of GMCs for anti-rubella antibodies at Day 42.	
Comparison groups	Com_MMR Group v Inv_MMR_Min Group
Number of subjects included in analysis	2735
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Method	ANOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.89
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.83
upper limit	0.95

Notes:

[15] - The lower limit of the 2-sided 97.5% CI on the group ratio of GMCs (Inv_MMR_Min over pooled Com_MMR) should to be ≥ 0.67 for antibodies to rubella virus when tested with ELISA.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Non-inferiority of Inv_MMR_Med vaccine compared to COM_MMR vaccine in terms of GMCs for anti-rubella antibodies at Day 42.	
Comparison groups	Com_MMR Group v Inv_MMR_Med Group
Number of subjects included in analysis	2742
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Method	ANOVA
Parameter estimate	Adjusted GMC ratio
Point estimate	0.88
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.83
upper limit	0.95

Notes:

[16] - The lower limit of the 2-sided 97.5% CI on the group ratio of GMCs (Inv_MMR_Med over pooled Com_MMR) should to be ≥ 0.67 for antibodies to rubella virus when tested with ELISA.

Secondary: Percentage of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value (by ELISA)

End point title	Percentage of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value (by ELISA)

End point description:

For measles virus, a seroresponse was defined as post-vaccination anti-measles virus antibody concentration ≥ 200 mIU/mL (ELISA) among subjects who were seronegative (antibody concentration < 150 mIU/mL) before dose 1.

End point type	Secondary

End point timeframe:

At Day 84

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	245	258	257	
Units: Percentage of subjects				
number (confidence interval 95%)				
≥ 150 mIU/mL	99.6 (97.7 to 100)	98.8 (96.6 to 99.8)	98.8 (96.6 to 99.8)	
≥ 200 mIU/mL	99.6 (97.7 to 100)	98.4 (96.1 to 99.6)	98.4 (96.1 to 99.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value (by ELISA)

End point title	Percentage of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value (by ELISA)

End point description:

For mumps virus, a seroresponse was defined as post-vaccination anti-mumps virus antibody concentration ≥ 10 EU/mL (ELISA) among subjects who were seronegative (antibody concentration < 5 EU/mL) before dose 1.

End point type	Secondary

End point timeframe:

At Day 84

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	216	199	212	
Units: Percentage of subjects				
number (confidence interval 95%)				
≥ 5 EU/mL	99.1 (96.7 to 99.9)	100 (98.2 to 100)	99.1 (96.6 to 99.9)	

≥ 10 EU/mL	99.1 (96.7 to 99.9)	100 (98.2 to 100)	98.6 (95.9 to 99.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value (by ELISA)

End point title	Percentage of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value (by ELISA)

End point description:

For rubella virus, a seroresponse was defined as post-vaccination anti-rubella virus antibody concentration ≥ 10 IU/mL (ELISA) among subjects who were seronegative (antibody concentration < 4 IU/mL) before dose 1.

End point type	Secondary

End point timeframe:

At Day 84

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	245	259	255	
Units: Percentage of subjects				
number (confidence interval 95%)				
≥ 4 IU/mL	100 (98.5 to 100)	100 (98.6 to 100)	100 (98.6 to 100)	
≥ 10 IU/mL	99.6 (97.7 to 100)	99.6 (97.9 to 100)	99.6 (97.8 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-measles virus antibody concentrations (by ELISA)

End point title	Anti-measles virus antibody concentrations (by ELISA)

End point description:

Antibody concentrations were expressed as GMCs in mIU/mL.

End point type	Secondary

End point timeframe:

At Day 84

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	245	258	257	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
mIU/mL	4803.5 (4290.4 to 5378.0)	4557.7 (4061.5 to 5114.4)	4453.9 (3951.9 to 5019.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-mumps virus antibody concentrations (by ELISA)

End point title	Anti-mumps virus antibody concentrations (by ELISA)
End point description:	
Antibody concentrations were expressed as GMCs in EU/mL.	
End point type	Secondary
End point timeframe:	
At Day 84	

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	216	199	212	
Units: EU/mL				
geometric mean (confidence interval 95%)				
EU/mL	88.9 (80.4 to 98.3)	94.1 (85.3 to 103.8)	86.4 (77.4 to 96.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rubella virus antibody concentrations (by ELISA)

End point title	Anti-rubella virus antibody concentrations (by ELISA)
End point description:	
Antibody concentrations were expressed as GMCs in IU/mL.	
End point type	Secondary
End point timeframe:	
At Day 84	

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	245	259	255	
Units: IU/mL				
geometric mean (confidence interval 95%)				
IU/mL	112.7 (104.1 to 122.0)	110.7 (102.9 to 119.1)	110.9 (101.8 to 120.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local adverse events (AEs) post dose 1

End point title	Number of subjects with any solicited local adverse events (AEs) post dose 1

End point description:

Assessed solicited local AEs were pain, redness and swelling. Any = Occurrence of the AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1453	1464	1482	
Units: Participants				
Any pain	261	262	301	
Any redness	232	256	286	
Any swelling	89	97	122	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local AEs post dose 2

End point title	Number of subjects with any solicited local AEs post dose 2

End point description:

Assessed solicited local AEs were pain, redness and swelling. Any = Occurrence of the AE regardless of

intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1427	1440	1456	
Units: Participants				
Any pain	170	183	196	
Any redness	159	196	217	
Any swelling	67	91	96	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general AEs post dose 1

End point title	Number of subjects with any solicited general AEs post dose 1

End point description:

Assessed solicited general AEs were drowsiness, irritability/fussiness and loss of appetite. Any = Occurrence of the AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 15-day (Days 0-14) post-vaccination period

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1454	1466	1486	
Units: Participants				
Any drowsiness	551	565	582	
Any irritability / fussiness	749	792	788	
Any loss of appetite	570	589	591	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any fever post dose 1

End point title	Number of subjects reporting any fever post dose 1

End point description: Any fever = Fever (axillary) ≥ 38°C.	
End point type	Secondary
End point timeframe: During the 43-day (Days 0-42) post-vaccination period	

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1454	1466	1486	
Units: Participants				
Participants	582	617	618	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any fever post dose 2

End point title	Number of subjects reporting any fever post dose 2
End point description: Any fever = Fever (axillary) ≥ 38°C.	
End point type	Secondary
End point timeframe: During the 43-day (Days 0-42) post-vaccination period	

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1426	1443	1455	
Units: Participants				
Participants	458	471	499	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any rash post dose 1

End point title	Number of subjects reporting any rash post dose 1

End point description:

Assessed were any localized or generalized rash, rash with fever, varicella-like rash and measles/rubella-like rash. Any = Occurrence of the AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1454	1466	1486	
Units: Participants				
Any localized or generalized	328	322	333	
Any with fever	115	133	131	
Any varicella like	57	53	45	
Any measles/rubella like	53	61	68	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any rash post dose 2

End point title	Number of subjects reporting any rash post dose 2

End point description:

Assessed were any localized or generalized rash, rash with fever, varicella-like rash and measles/rubella-like rash. Any = Occurrence of the AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1426	1443	1455	
Units: Participants				
Any localized or generalized	129	150	141	
Any with fever	52	63	53	
Any varicella like	0	0	1	
Any measles/rubella like	22	14	14	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any MMR specific solicited general AEs post dose 1

End point title	Number of subjects reporting any MMR specific solicited general AEs post dose 1

End point description:

Assessed MMR specific solicited general AEs were any suspected signs of meningism including febrile convulsions and parotid/salivary gland swelling. Any = Occurrence of the AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1454	1466	1486	
Units: Participants				
Any parotid gland swelling	3	2	3	
Any febrile convulsion	3	4	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any MMR specific solicited general AEs post dose 2

End point title	Number of subjects reporting any MMR specific solicited general AEs post dose 2

End point description:

Assessed MMR specific solicited general AEs were any suspected signs of meningism including febrile convulsions and parotid/salivary gland swelling. Any = Occurrence of the AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1426	1443	1455	
Units: Participants				
Any parotid gland swelling	1	2	0	
Any febrile convulsion	2	6	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited AES post dose 1

End point title	Number of subjects reporting any unsolicited AES post dose 1

End point description:

Unsolicited AE was defined as any AE reported in reported in addition to those solicited during the clinical study and any solicited AE with onset outside the specified period of follow-up for solicited AEs. Any = Occurrence of the AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1493	1497	1526	
Units: Participants				
Participants	762	794	777	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited AES post dose 2

End point title	Number of subjects reporting any unsolicited AES post dose 2

End point description:

Unsolicited AE was defined as any AE reported in reported in addition to those solicited during the clinical study and any solicited AE with onset outside the specified period of follow-up for solicited AEs. Any = Occurrence of the AE regardless of intensity grade or relation to vaccination.

End point type	Secondary

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1449	1464	1483	
Units: Participants				
Participants	667	703	690	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any AEs of specific interest

End point title	Number of subjects reporting any AEs of specific interest

End point description:

AEs of specific interest included new onset chronic disease (NOCD) (e.g., autoimmune disorders, asthma, type I diabetes, vasculitis, celiac disease, conditions associated with sub-acute or chronic thrombocytopenia and allergies) and AEs prompting emergency room (ER) visits.

End point type	Secondary

End point timeframe:

From Day 0 through the end of the study (Day 222)

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1493	1497	1526	
Units: Participants				
Any NOCD	35	39	33	
Any AE prompting ER visit	348	361	347	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

SAEs assessed include any untoward medical occurrences that resulted in death, were life-threatening, required hospitalization or prolongation of existing hospitalization or resulted in disability/incapacity.

End point type	Secondary

End point timeframe:

From Day 0 through the end of the study (Day 222)

End point values	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1493	1497	1526	
Units: Participants				
Participants	91	102	92	

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Solicited local & general AEs: During the 4-day (Days 0-3) and 15-day (Days 0-14) post-vaccination period, respectively; Unsolicited AEs: During the 43-day (Days 0-42) post-vaccination period; SAEs: From Day 0 through the end of the study (Day 222).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Inv_MMR_Min Group

Reporting group description:

Subjects received one dose of Inv_MMR, from a minimum potency lot (Inv_MMR_Min), co-administered with VV and HAV vaccines at Day 0. All US subjects were also co-administered PCV-13 vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose from a separate lot of the Inv_MMR vaccine (Inv_MMR_Release), for the second dose. Inv_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Reporting group title	Inv_MMR_Med Group

Reporting group description:

Subjects received one dose of Inv_MMR, from a mid-range or medium potency lot (Inv_MMR_Med), co-administered with VV and HAV vaccines at Day 0. All US subjects were also co-administered PCV-13 vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose from a separate lot of the Inv_MMR vaccine (Inv_MMR_Release), for the second dose. Inv_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Reporting group title	Com_MMR Group

Reporting group description:

Subjects received one dose of Com_MMR vaccine (Lot 1 or Lot 2), co-administered with VV and HAV vaccines at Day 0. All US subjects were also co-administered PCV-13 vaccine. Approximately 6 weeks later, at Day 42, subjects were administered a dose of Com_MMR vaccine (Lot 1 or Lot 2), for the second dose. Com_MMR and VV vaccines were administered subcutaneously in the triceps region of the left and right arm, respectively. HAV and PCV-13 vaccines were administered intramuscularly in the anterolateral region of the right and left thigh, respectively.

Serious adverse events	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group
Total subjects affected by serious adverse events			
subjects affected / exposed	91 / 1493 (6.10%)	102 / 1497 (6.81%)	92 / 1526 (6.03%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Phlebitis superficial			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Drowning			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Influenza like illness			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 1493 (0.07%)	4 / 1497 (0.27%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 1	1 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			

subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental poisoning			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burns second degree			

subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest injury			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Child maltreatment syndrome			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face injury			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			

subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb crushing injury			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth injury			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Poisoning			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	3 / 1526 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			

subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Burning sensation			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	7 / 1493 (0.47%)	13 / 1497 (0.87%)	8 / 1526 (0.52%)
occurrences causally related to treatment / all	0 / 8	0 / 15	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Haemolytic anaemia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypochromic anaemia			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 1493 (0.00%)	3 / 1497 (0.20%)	2 / 1526 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	0 / 1493 (0.00%)	3 / 1497 (0.20%)	4 / 1526 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	3 / 1493 (0.20%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perianal erythema			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Teething			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Liver disorder			

subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Henoch-schonlein purpura			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Petechiae			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stevens-johnson syndrome			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic skin eruption			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			

subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Juvenile idiopathic arthritis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	6 / 1493 (0.40%)	7 / 1497 (0.47%)	2 / 1526 (0.13%)
occurrences causally related to treatment / all	0 / 6	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchitis			
subjects affected / exposed	4 / 1493 (0.27%)	10 / 1497 (0.67%)	8 / 1526 (0.52%)
occurrences causally related to treatment / all	0 / 5	0 / 10	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis viral			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 1493 (0.07%)	2 / 1497 (0.13%)	2 / 1526 (0.13%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis orbital			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctivitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious			
subjects affected / exposed	2 / 1493 (0.13%)	3 / 1497 (0.20%)	4 / 1526 (0.26%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis klebsiella			

subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	3 / 1526 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis brain stem			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal bacteraemia			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			

subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exanthema subitum			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	16 / 1493 (1.07%)	19 / 1497 (1.27%)	10 / 1526 (0.66%)
occurrences causally related to treatment / all	0 / 16	0 / 19	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis bacterial			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	6 / 1493 (0.40%)	3 / 1497 (0.20%)	7 / 1526 (0.46%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	2 / 1526 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand-foot-and-mouth disease			
subjects affected / exposed	2 / 1493 (0.13%)	2 / 1497 (0.13%)	4 / 1526 (0.26%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpangina			

subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	3 / 1526 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	3 / 1493 (0.20%)	2 / 1497 (0.13%)	2 / 1526 (0.13%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	4 / 1526 (0.26%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngotracheitis obstructive			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nail bed infection			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	2 / 1493 (0.13%)	3 / 1497 (0.20%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nosocomial infection			

subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	3 / 1493 (0.20%)	3 / 1497 (0.20%)	2 / 1526 (0.13%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media viral			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otosalpingitis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	3 / 1493 (0.20%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	2 / 1493 (0.13%)	5 / 1497 (0.33%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	7 / 1493 (0.47%)	14 / 1497 (0.94%)	10 / 1526 (0.66%)
occurrences causally related to treatment / all	0 / 7	0 / 14	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 1493 (0.07%)	2 / 1497 (0.13%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	3 / 1493 (0.20%)	1 / 1497 (0.07%)	2 / 1526 (0.13%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	2 / 1493 (0.13%)	6 / 1497 (0.40%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchitis			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			

subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinitis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin candida			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			

subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	2 / 1493 (0.13%)	3 / 1497 (0.20%)	3 / 1526 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	3 / 1493 (0.20%)	1 / 1497 (0.07%)	2 / 1526 (0.13%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral pharyngitis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral tonsillitis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	4 / 1493 (0.27%)	7 / 1497 (0.47%)	6 / 1526 (0.39%)
occurrences causally related to treatment / all	0 / 5	0 / 7	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Inv_MMR_Min Group	Inv_MMR_Med Group	Com_MMR Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1299 / 1493 (87.01%)	1311 / 1497 (87.58%)	1330 / 1526 (87.16%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Haemangioma			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Melanocytic naevus			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Pyogenic granuloma			

subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Perinatal brain damage			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Application site erythema			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	2 / 1526 (0.13%)
occurrences (all)	0	1	2
Application site hypersensitivity			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Crying			
subjects affected / exposed	4 / 1493 (0.27%)	4 / 1497 (0.27%)	5 / 1526 (0.33%)
occurrences (all)	5	4	7
Decreased activity			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Discomfort			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	0	2	0
Fatigue			

subjects affected / exposed	2 / 1493 (0.13%)	2 / 1497 (0.13%)	1 / 1526 (0.07%)
occurrences (all)	2	3	1
Feeling hot			
subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	2	1	0
Gait disturbance			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	1	1	1
Influenza like illness			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	1	1	1
Injection site bruising			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	0	0	3
Injection site erythema			
subjects affected / exposed	11 / 1493 (0.74%)	15 / 1497 (1.00%)	9 / 1526 (0.59%)
occurrences (all)	11	15	9
Injection site haematoma			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	3 / 1526 (0.20%)
occurrences (all)	0	0	3
Injection site haemorrhage			
subjects affected / exposed	0 / 1493 (0.00%)	3 / 1497 (0.20%)	0 / 1526 (0.00%)
occurrences (all)	0	3	0
Injection site induration			
subjects affected / exposed	2 / 1493 (0.13%)	4 / 1497 (0.27%)	2 / 1526 (0.13%)
occurrences (all)	2	4	2
Injection site inflammation			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Injection site mass			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Injection site nodule			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Injection site pain			

subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	2	1	1
Injection site papule			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Injection site reaction			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	1	1	0
Injection site swelling			
subjects affected / exposed	3 / 1493 (0.20%)	5 / 1497 (0.33%)	2 / 1526 (0.13%)
occurrences (all)	3	5	2
Injection site urticaria			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Local swelling			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	0	1	1
Malaise			
subjects affected / exposed	3 / 1493 (0.20%)	2 / 1497 (0.13%)	2 / 1526 (0.13%)
occurrences (all)	3	3	4
Mass			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	334 / 1493 (22.37%)	336 / 1497 (22.44%)	378 / 1526 (24.77%)
occurrences (all)	431	445	500
Peripheral swelling			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	0	1	1
Swelling			
subjects affected / exposed	123 / 1493 (8.24%)	152 / 1497 (10.15%)	170 / 1526 (11.14%)
occurrences (all)	156	188	218

Vaccination site erythema			
subjects affected / exposed	7 / 1493 (0.47%)	6 / 1497 (0.40%)	8 / 1526 (0.52%)
occurrences (all)	7	6	8
Vaccination site haematoma			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Vaccination site pain			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Vaccination site rash			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Vaccination site reaction			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Vaccination site swelling			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	1	1	1
Vessel puncture site haemorrhage			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Allergy to animal			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Drug hypersensitivity			
subjects affected / exposed	1 / 1493 (0.07%)	2 / 1497 (0.13%)	3 / 1526 (0.20%)
occurrences (all)	1	2	3
Food allergy			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	1	1	0
Hypersensitivity			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	2	0	0
Milk allergy			

subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Multiple allergies			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	0	1	1
Seasonal allergy			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	2 / 1493 (0.13%)	3 / 1497 (0.20%)	1 / 1526 (0.07%)
occurrences (all)	2	3	2
Genital erythema			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Genital labial adhesions			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Penile adhesion			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	2	0	2
Penile erythema			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Perineal erythema			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Scrotal swelling			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Testicular pain			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	1 / 1493 (0.07%)	5 / 1497 (0.33%)	3 / 1526 (0.20%)
occurrences (all)	2	5	3
Bronchial hyperreactivity			
subjects affected / exposed	7 / 1493 (0.47%)	4 / 1497 (0.27%)	8 / 1526 (0.52%)
occurrences (all)	8	5	9
Bronchospasm			
subjects affected / exposed	7 / 1493 (0.47%)	3 / 1497 (0.20%)	2 / 1526 (0.13%)
occurrences (all)	7	3	2
Catarrh			
subjects affected / exposed	1 / 1493 (0.07%)	2 / 1497 (0.13%)	2 / 1526 (0.13%)
occurrences (all)	1	2	3
Cough			
subjects affected / exposed	59 / 1493 (3.95%)	64 / 1497 (4.28%)	75 / 1526 (4.91%)
occurrences (all)	68	74	84
Dysphonia			
subjects affected / exposed	0 / 1493 (0.00%)	3 / 1497 (0.20%)	0 / 1526 (0.00%)
occurrences (all)	0	3	0
Epistaxis			
subjects affected / exposed	2 / 1493 (0.13%)	4 / 1497 (0.27%)	2 / 1526 (0.13%)
occurrences (all)	3	4	2
Lower respiratory tract congestion			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	9 / 1493 (0.60%)	12 / 1497 (0.80%)	10 / 1526 (0.66%)
occurrences (all)	9	12	12
Oropharyngeal pain			
subjects affected / exposed	1 / 1493 (0.07%)	3 / 1497 (0.20%)	3 / 1526 (0.20%)
occurrences (all)	1	3	6
Productive cough			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	0	3	0
Respiratory tract congestion			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0

Rhinitis allergic			
subjects affected / exposed	4 / 1493 (0.27%)	0 / 1497 (0.00%)	6 / 1526 (0.39%)
occurrences (all)	4	0	6
Rhinorrhoea			
subjects affected / exposed	32 / 1493 (2.14%)	25 / 1497 (1.67%)	39 / 1526 (2.56%)
occurrences (all)	39	33	41
Sinus congestion			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Sinus disorder			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	1	0	1
Sleep apnoea syndrome			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Sneezing			
subjects affected / exposed	2 / 1493 (0.13%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	2	2	0
Throat irritation			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	3 / 1493 (0.20%)	9 / 1497 (0.60%)	7 / 1526 (0.46%)
occurrences (all)	3	9	7
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Bruxism			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 1493 (0.07%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	1	2	0
Irritability			

subjects affected / exposed	757 / 1493 (50.70%)	795 / 1497 (53.11%)	793 / 1526 (51.97%)
occurrences (all)	781	815	815
Mood altered			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Nervousness			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Restlessness			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	2	0	1
Tearfulness			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Product issues			
Device occlusion			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Body temperature increased			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	1	1	0
Cardiac murmur			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Gastric ph decreased			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Staphylococcus test positive			

subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Accidental exposure to product			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Animal bite			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	1	0	2
Arthropod bite			
subjects affected / exposed	24 / 1493 (1.61%)	21 / 1497 (1.40%)	12 / 1526 (0.79%)
occurrences (all)	29	23	13
Arthropod sting			
subjects affected / exposed	3 / 1493 (0.20%)	2 / 1497 (0.13%)	1 / 1526 (0.07%)
occurrences (all)	3	2	1
Burns second degree			
subjects affected / exposed	0 / 1493 (0.00%)	3 / 1497 (0.20%)	1 / 1526 (0.07%)
occurrences (all)	0	3	1
Contusion			
subjects affected / exposed	8 / 1493 (0.54%)	7 / 1497 (0.47%)	9 / 1526 (0.59%)
occurrences (all)	9	8	9
Ear canal abrasion			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Excoriation			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	0	1	1
Exposure to communicable disease			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Exposure to toxic agent			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Eye injury			

subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	1 / 1526 (0.07%)
occurrences (all)	0	2	1
Eyelid injury			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	1 / 1526 (0.07%)
occurrences (all)	0	2	1
Face injury			
subjects affected / exposed	0 / 1493 (0.00%)	3 / 1497 (0.20%)	0 / 1526 (0.00%)
occurrences (all)	0	3	0
Fall			
subjects affected / exposed	3 / 1493 (0.20%)	4 / 1497 (0.27%)	7 / 1526 (0.46%)
occurrences (all)	5	4	8
Foot fracture			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Foreign body			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Head injury			
subjects affected / exposed	8 / 1493 (0.54%)	7 / 1497 (0.47%)	7 / 1526 (0.46%)
occurrences (all)	8	7	7
Injury			
subjects affected / exposed	2 / 1493 (0.13%)	2 / 1497 (0.13%)	4 / 1526 (0.26%)
occurrences (all)	2	2	4
Joint dislocation			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Laceration			
subjects affected / exposed	3 / 1493 (0.20%)	6 / 1497 (0.40%)	7 / 1526 (0.46%)
occurrences (all)	3	6	7
Limb injury			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	1	1	1
Lip injury			
subjects affected / exposed	2 / 1493 (0.13%)	4 / 1497 (0.27%)	1 / 1526 (0.07%)
occurrences (all)	2	4	1
Mouth injury			

subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	2	1	1
Procedural vomiting			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Radial head dislocation			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	0	0	2
Radius fracture			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Road traffic accident			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	1	0	2
Skin abrasion			
subjects affected / exposed	2 / 1493 (0.13%)	5 / 1497 (0.33%)	5 / 1526 (0.33%)
occurrences (all)	2	5	5
Skin wound			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	1	1	0
Thermal burn			
subjects affected / exposed	2 / 1493 (0.13%)	4 / 1497 (0.27%)	4 / 1526 (0.26%)
occurrences (all)	2	4	4
Tibia fracture			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Tongue injury			
subjects affected / exposed	1 / 1493 (0.07%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	1	2	0
Tooth fracture			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Tooth injury			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	2 / 1526 (0.13%)
occurrences (all)	0	1	2
Vaccination complication			

subjects affected / exposed	0 / 1493 (0.00%)	3 / 1497 (0.20%)	2 / 1526 (0.13%)
occurrences (all)	0	3	2
Wound			
subjects affected / exposed	4 / 1493 (0.27%)	10 / 1497 (0.67%)	5 / 1526 (0.33%)
occurrences (all)	4	10	5
Congenital, familial and genetic disorders			
Dermoid cyst			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Inborn error of metabolism			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Keratosis follicular			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Naevus flammeus			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Phimosis			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	1 / 1526 (0.07%)
occurrences (all)	0	2	1
Talipes			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Nervous system disorders			
Aphonia			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	1	1	1
Cerebrovascular accident			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Drooling			

subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	1	0	1
Headache			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Language disorder			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	2	1	0
Poor quality sleep			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	0	1	1
Psychomotor hyperactivity			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Sleep phase rhythm disturbance			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	551 / 1493 (36.91%)	567 / 1497 (37.88%)	582 / 1526 (38.14%)
occurrences (all)	552	569	582
Syncope			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Tongue biting			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 1493 (0.40%)	5 / 1497 (0.33%)	4 / 1526 (0.26%)
occurrences (all)	6	5	4
Hypochromic anaemia			

subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 1493 (0.00%)	3 / 1497 (0.20%)	1 / 1526 (0.07%)
occurrences (all)	0	3	1
Lymphadenitis			
subjects affected / exposed	2 / 1493 (0.13%)	2 / 1497 (0.13%)	2 / 1526 (0.13%)
occurrences (all)	2	2	2
Lymphadenopathy			
subjects affected / exposed	8 / 1493 (0.54%)	5 / 1497 (0.33%)	2 / 1526 (0.13%)
occurrences (all)	8	5	2
Thrombocytosis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	2	1	0
Ear disorder			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	1	0	1
Ear pain			
subjects affected / exposed	6 / 1493 (0.40%)	7 / 1497 (0.47%)	6 / 1526 (0.39%)
occurrences (all)	6	7	6
Middle ear inflammation			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Otorrhoea			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	3 / 1526 (0.20%)
occurrences (all)	1	1	4
Tympanic membrane perforation			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	0	0	2
Eye disorders			
Blepharitis			

subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Conjunctival hyperaemia			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	0	3	0
Eye discharge			
subjects affected / exposed	1 / 1493 (0.07%)	2 / 1497 (0.13%)	3 / 1526 (0.20%)
occurrences (all)	1	2	3
Eye oedema			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Eye swelling			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Eyelid bleeding			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Eyelid cyst			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Eyelid oedema			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	0	2	0
Keratitis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	0	2	0
Abdominal distension			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	3 / 1493 (0.20%)	2 / 1497 (0.13%)	3 / 1526 (0.20%)
occurrences (all)	3	3	3
Abdominal pain upper			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	1	1	0
Anal fissure			
subjects affected / exposed	3 / 1493 (0.20%)	3 / 1497 (0.20%)	3 / 1526 (0.20%)
occurrences (all)	3	3	3
Aphthous ulcer			
subjects affected / exposed	6 / 1493 (0.40%)	7 / 1497 (0.47%)	3 / 1526 (0.20%)
occurrences (all)	6	7	3
Cheilitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Colitis			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	0	2	0
Constipation			
subjects affected / exposed	11 / 1493 (0.74%)	11 / 1497 (0.73%)	6 / 1526 (0.39%)
occurrences (all)	11	13	6
Diarrhoea			
subjects affected / exposed	73 / 1493 (4.89%)	71 / 1497 (4.74%)	75 / 1526 (4.91%)
occurrences (all)	83	76	80
Dyspepsia			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	1 / 1526 (0.07%)
occurrences (all)	0	2	1
Enteritis			
subjects affected / exposed	19 / 1493 (1.27%)	21 / 1497 (1.40%)	19 / 1526 (1.25%)
occurrences (all)	19	23	20

Enterocolitis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Faeces discoloured			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Food poisoning			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	1	0	1
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	3 / 1526 (0.20%)
occurrences (all)	2	0	3
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 1493 (0.13%)	2 / 1497 (0.13%)	2 / 1526 (0.13%)
occurrences (all)	2	2	2
Gingival disorder			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Gingival pain			
subjects affected / exposed	4 / 1493 (0.27%)	4 / 1497 (0.27%)	2 / 1526 (0.13%)
occurrences (all)	5	4	2
Glossodynia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Haematochezia			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	2 / 1526 (0.13%)
occurrences (all)	1	1	3
Haemorrhoids			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1

Inguinal hernia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Lip disorder			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Lip ulceration			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Malocclusion			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	2 / 1526 (0.13%)
occurrences (all)	1	1	2
Nausea			
subjects affected / exposed	1 / 1493 (0.07%)	2 / 1497 (0.13%)	2 / 1526 (0.13%)
occurrences (all)	1	2	2
Noninfective gingivitis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	2	0	0
Oral disorder			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Palatal ulcer			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Periodontal disease			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Protein-losing gastroenteropathy			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Regurgitation			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	2	0	0

Salivary gland enlargement			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Salivary hypersecretion			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	3 / 1493 (0.20%)	6 / 1497 (0.40%)	3 / 1526 (0.20%)
occurrences (all)	3	6	3
Teething			
subjects affected / exposed	62 / 1493 (4.15%)	71 / 1497 (4.74%)	64 / 1526 (4.19%)
occurrences (all)	86	104	82
Tongue blistering			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Tooth discolouration			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Tooth disorder			
subjects affected / exposed	3 / 1493 (0.20%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	4	2	0
Toothache			
subjects affected / exposed	22 / 1493 (1.47%)	17 / 1497 (1.14%)	17 / 1526 (1.11%)
occurrences (all)	31	21	22
Vomiting			
subjects affected / exposed	43 / 1493 (2.88%)	42 / 1497 (2.81%)	48 / 1526 (3.15%)
occurrences (all)	55	45	51
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Angioedema			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Dermal cyst			

subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
subjects affected / exposed	9 / 1493 (0.60%)	9 / 1497 (0.60%)	17 / 1526 (1.11%)
occurrences (all)	9	10	17
Dermatitis allergic			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	1 / 1526 (0.07%)
occurrences (all)	0	2	1
Dermatitis atopic			
subjects affected / exposed	15 / 1493 (1.00%)	14 / 1497 (0.94%)	13 / 1526 (0.85%)
occurrences (all)	16	16	15
Dermatitis contact			
subjects affected / exposed	3 / 1493 (0.20%)	2 / 1497 (0.13%)	3 / 1526 (0.20%)
occurrences (all)	3	2	3
Dermatitis diaper			
subjects affected / exposed	12 / 1493 (0.80%)	18 / 1497 (1.20%)	21 / 1526 (1.38%)
occurrences (all)	12	19	21
Ecchymosis			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	1	1	0
Eczema			
subjects affected / exposed	16 / 1493 (1.07%)	7 / 1497 (0.47%)	7 / 1526 (0.46%)
occurrences (all)	16	7	9
Erythema			
subjects affected / exposed	288 / 1493 (19.29%)	331 / 1497 (22.11%)	362 / 1526 (23.72%)
occurrences (all)	394	455	505
Erythema multiforme			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Ingrowing nail			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Intertrigo			
subjects affected / exposed	3 / 1493 (0.20%)	2 / 1497 (0.13%)	2 / 1526 (0.13%)
occurrences (all)	4	2	2

Macule			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	2	0	0
Miliaria			
subjects affected / exposed	6 / 1493 (0.40%)	4 / 1497 (0.27%)	4 / 1526 (0.26%)
occurrences (all)	6	4	4
Nail disorder			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Onychomadesis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	2 / 1526 (0.13%)
occurrences (all)	0	1	2
Petechiae			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Prurigo			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	1	1	0
Pruritus			
subjects affected / exposed	0 / 1493 (0.00%)	3 / 1497 (0.20%)	0 / 1526 (0.00%)
occurrences (all)	0	3	0
Rash macular			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Rash papular			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Rash vesicular			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Seborrhoeic dermatitis			
subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	2	1	1

Skin burning sensation			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Skin discolouration			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Skin irritation			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	0	0	2
Skin lesion			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	2	0
Skin ulcer			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	0	2	0
Skin warm			
subjects affected / exposed	1 / 1493 (0.07%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	1	2	0
Spider naevus			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Swelling face			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	4 / 1493 (0.27%)	5 / 1497 (0.33%)	3 / 1526 (0.20%)
occurrences (all)	4	5	3
Musculoskeletal and connective tissue disorders			
Foot deformity			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Neck mass			

subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	2	1	0
Synovitis			
subjects affected / exposed	3 / 1493 (0.20%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	4	0	1
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	0	0	2
Acarodermatitis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Acute sinusitis			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	2	0	0
Adenoiditis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	1	0	1
Adenoviral conjunctivitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Adenovirus infection			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Angular cheilitis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Body tinea			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	1	0	1
Bronchiolitis			
subjects affected / exposed	18 / 1493 (1.21%)	22 / 1497 (1.47%)	21 / 1526 (1.38%)
occurrences (all)	22	22	22

Bronchitis			
subjects affected / exposed	81 / 1493 (5.43%)	96 / 1497 (6.41%)	77 / 1526 (5.05%)
occurrences (all)	92	115	95
Bronchitis viral			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	0	1	1
Bullous impetigo			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Burn infection			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	2 / 1526 (0.13%)
occurrences (all)	0	2	2
Campylobacter infection			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	6 / 1493 (0.40%)	9 / 1497 (0.60%)	7 / 1526 (0.46%)
occurrences (all)	7	9	7
Candida nappy rash			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	3 / 1526 (0.20%)
occurrences (all)	0	2	3
Conjunctivitis			
subjects affected / exposed	63 / 1493 (4.22%)	79 / 1497 (5.28%)	79 / 1526 (5.18%)
occurrences (all)	67	90	87
Conjunctivitis bacterial			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis viral			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0

Coxsackie viral infection			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	0	0	2
Croup infectious			
subjects affected / exposed	4 / 1493 (0.27%)	11 / 1497 (0.73%)	12 / 1526 (0.79%)
occurrences (all)	4	11	13
Cryptosporidiosis infection			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	1	0	1
Ear infection			
subjects affected / exposed	19 / 1493 (1.27%)	19 / 1497 (1.27%)	12 / 1526 (0.79%)
occurrences (all)	19	20	13
Eczema impetiginous			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Enterobiasis			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	0	2	0
Enterovirus infection			
subjects affected / exposed	3 / 1493 (0.20%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	3	1	0
Erythema infectiosum			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	1	0	1
Exanthema subitum			
subjects affected / exposed	2 / 1493 (0.13%)	5 / 1497 (0.33%)	1 / 1526 (0.07%)
occurrences (all)	2	5	1
Eye infection			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	3 / 1493 (0.20%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	3	0	0

Fungal infection			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	2	0	0
Fungal skin infection			
subjects affected / exposed	1 / 1493 (0.07%)	3 / 1497 (0.20%)	0 / 1526 (0.00%)
occurrences (all)	1	3	0
Furuncle			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Gastritis viral			
subjects affected / exposed	3 / 1493 (0.20%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	4	0	2
Gastroenteritis			
subjects affected / exposed	88 / 1493 (5.89%)	95 / 1497 (6.35%)	93 / 1526 (6.09%)
occurrences (all)	93	107	100
Gastroenteritis norovirus			
subjects affected / exposed	0 / 1493 (0.00%)	2 / 1497 (0.13%)	0 / 1526 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis salmonella			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	0	1	1
Gastroenteritis viral			
subjects affected / exposed	7 / 1493 (0.47%)	6 / 1497 (0.40%)	9 / 1526 (0.59%)
occurrences (all)	7	6	9
Genital candidiasis			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	2	0	0
Gingivitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	0	0	2
Hand-foot-and-mouth disease			
subjects affected / exposed	10 / 1493 (0.67%)	23 / 1497 (1.54%)	10 / 1526 (0.66%)
occurrences (all)	10	23	11
Herpangina			
subjects affected / exposed	9 / 1493 (0.60%)	8 / 1497 (0.53%)	8 / 1526 (0.52%)
occurrences (all)	9	8	8

Herpes virus infection			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	1	0	1
Hordeolum			
subjects affected / exposed	3 / 1493 (0.20%)	3 / 1497 (0.20%)	1 / 1526 (0.07%)
occurrences (all)	3	3	1
Impetigo			
subjects affected / exposed	6 / 1493 (0.40%)	7 / 1497 (0.47%)	9 / 1526 (0.59%)
occurrences (all)	6	7	9
Infected bite			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	0	1	1
Influenza			
subjects affected / exposed	7 / 1493 (0.47%)	11 / 1497 (0.73%)	10 / 1526 (0.66%)
occurrences (all)	8	13	10
Laryngitis			
subjects affected / exposed	34 / 1493 (2.28%)	34 / 1497 (2.27%)	27 / 1526 (1.77%)
occurrences (all)	35	37	30
Lice infestation			
subjects affected / exposed	0 / 1493 (0.00%)	4 / 1497 (0.27%)	0 / 1526 (0.00%)
occurrences (all)	0	4	0
Localised infection			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	2	0	1
Lower respiratory tract infection			
subjects affected / exposed	4 / 1493 (0.27%)	4 / 1497 (0.27%)	5 / 1526 (0.33%)
occurrences (all)	4	5	5
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	1	1	0
Mastitis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Molluscum contagiosum			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0

Mycoplasma infection			
subjects affected / exposed	5 / 1493 (0.33%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	5	0	1
Nasopharyngitis			
subjects affected / exposed	148 / 1493 (9.91%)	176 / 1497 (11.76%)	134 / 1526 (8.78%)
occurrences (all)	177	210	154
Oral candidiasis			
subjects affected / exposed	7 / 1493 (0.47%)	1 / 1497 (0.07%)	8 / 1526 (0.52%)
occurrences (all)	7	1	8
Oral fungal infection			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	3 / 1493 (0.20%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	3	1	0
Orchitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Otitis externa			
subjects affected / exposed	5 / 1493 (0.33%)	3 / 1497 (0.20%)	3 / 1526 (0.20%)
occurrences (all)	5	3	3
Otitis media			
subjects affected / exposed	95 / 1493 (6.36%)	99 / 1497 (6.61%)	116 / 1526 (7.60%)
occurrences (all)	120	117	143
Otitis media acute			
subjects affected / exposed	46 / 1493 (3.08%)	49 / 1497 (3.27%)	57 / 1526 (3.74%)
occurrences (all)	55	60	65
Parasitic gastroenteritis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	1	0	1
Paronychia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	2 / 1526 (0.13%)
occurrences (all)	0	1	2
Periorbital cellulitis			

subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	50 / 1493 (3.35%)	53 / 1497 (3.54%)	55 / 1526 (3.60%)
occurrences (all)	61	56	57
Pharyngitis streptococcal			
subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	2	1	1
Pharyngotonsillitis			
subjects affected / exposed	14 / 1493 (0.94%)	15 / 1497 (1.00%)	17 / 1526 (1.11%)
occurrences (all)	15	16	17
Pneumonia			
subjects affected / exposed	5 / 1493 (0.33%)	8 / 1497 (0.53%)	9 / 1526 (0.59%)
occurrences (all)	5	8	9
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	1	1	1
Pneumonia viral			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Pseudocroup			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Pyelonephritis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Pyoderma			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 1493 (0.07%)	4 / 1497 (0.27%)	2 / 1526 (0.13%)
occurrences (all)	1	4	2

Respiratory tract infection			
subjects affected / exposed	24 / 1493 (1.61%)	24 / 1497 (1.60%)	22 / 1526 (1.44%)
occurrences (all)	25	28	30
Respiratory tract infection viral			
subjects affected / exposed	4 / 1493 (0.27%)	9 / 1497 (0.60%)	7 / 1526 (0.46%)
occurrences (all)	5	10	11
Rhinitis			
subjects affected / exposed	37 / 1493 (2.48%)	49 / 1497 (3.27%)	30 / 1526 (1.97%)
occurrences (all)	53	56	33
Rhinovirus infection			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Roseola			
subjects affected / exposed	1 / 1493 (0.07%)	3 / 1497 (0.20%)	0 / 1526 (0.00%)
occurrences (all)	1	3	0
Salmonellosis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Scarlet fever			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	11 / 1493 (0.74%)	10 / 1497 (0.67%)	7 / 1526 (0.46%)
occurrences (all)	12	10	7
Sinusitis bacterial			
subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	2	0	0
Skin bacterial infection			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	1	1	0
Skin candida			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0

Staphylococcal abscess			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Staphylococcal infection			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Streptococcal infection			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	0	1	1
Subcutaneous abscess			
subjects affected / exposed	2 / 1493 (0.13%)	1 / 1497 (0.07%)	3 / 1526 (0.20%)
occurrences (all)	2	1	3
Superinfection bacterial			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	34 / 1493 (2.28%)	24 / 1497 (1.60%)	34 / 1526 (2.23%)
occurrences (all)	36	27	36
Tonsillitis bacterial			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	0	1	0
Tracheitis			
subjects affected / exposed	1 / 1493 (0.07%)	3 / 1497 (0.20%)	2 / 1526 (0.13%)
occurrences (all)	1	3	2
Tracheobronchitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	350 / 1493 (23.44%)	354 / 1497 (23.65%)	365 / 1526 (23.92%)
occurrences (all)	475	473	485
Upper respiratory tract infection bacterial			

subjects affected / exposed	2 / 1493 (0.13%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	4 / 1493 (0.27%)	2 / 1497 (0.13%)	4 / 1526 (0.26%)
occurrences (all)	5	3	5
Varicella			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	0	1	1
Viral infection			
subjects affected / exposed	45 / 1493 (3.01%)	51 / 1497 (3.41%)	57 / 1526 (3.74%)
occurrences (all)	50	57	61
Viral pharyngitis			
subjects affected / exposed	5 / 1493 (0.33%)	2 / 1497 (0.13%)	3 / 1526 (0.20%)
occurrences (all)	5	2	3
Viral rash			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Viral rhinitis			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	3 / 1526 (0.20%)
occurrences (all)	0	1	3
Viral tonsillitis			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	1	1	1
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 1493 (0.13%)	6 / 1497 (0.40%)	11 / 1526 (0.72%)
occurrences (all)	2	6	12
Vulvitis			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Vulvovaginitis			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Wound infection			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	571 / 1493 (38.25%)	593 / 1497 (39.61%)	593 / 1526 (38.86%)
occurrences (all)	575	595	593
Dehydration			
subjects affected / exposed	1 / 1493 (0.07%)	1 / 1497 (0.07%)	0 / 1526 (0.00%)
occurrences (all)	1	1	0
Disaccharide metabolism disorder			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Failure to thrive			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	2 / 1526 (0.13%)
occurrences (all)	0	0	2
Feeding disorder			
subjects affected / exposed	1 / 1493 (0.07%)	0 / 1497 (0.00%)	0 / 1526 (0.00%)
occurrences (all)	1	0	0
Hyposideraemia			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	1 / 1526 (0.07%)
occurrences (all)	0	1	1
Lactase deficiency			
subjects affected / exposed	0 / 1493 (0.00%)	0 / 1497 (0.00%)	1 / 1526 (0.07%)
occurrences (all)	0	0	1
Lactose intolerance			
subjects affected / exposed	0 / 1493 (0.00%)	1 / 1497 (0.07%)	2 / 1526 (0.13%)
occurrences (all)	0	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 February 2014	• At CBER's request, the US non post dose 2 sub cohort was eliminated. This sub cohort was previously defined as any child enrolled in the US after the target enrollment of 1000 US children was met. These children would not have been required to have a blood sample taken post dose 2 as post dose 2 immunogenicity testing was only required in 1000 children. At CBER's request, the serologic response after each dose of both Merck's MMR-II and GSK's investigational vaccine will be evaluated in all US children. In the event that the pre-specified criteria for seroresponse are not met, U.S. children will be offered vaccination with MMR-II to assure protection from measles, mumps and rubella diseases. • Vaccination against influenza and haemophilus influenza type B can be given at any time before, during, or after the study, including the day of study vaccination. This is to correct a prior exclusion criterion which stated that it could be given at any time during the study. The intent has always been to allow these vaccinations at any time regardless of whether or not it was before, during or after the study period. • For other MMR US Phase III studies, CBER has requested that all conditions leading to non-routine medically attended visits be collected for the entire study in the eCRF. It has been clarified throughout the protocol that From Visit 1 (Day 0) to study end (Day 180), all medically attended events will be recorded in the eCRF. Subjects' routine 'well child' doctor visits will not be recorded in the eCRF.
19 May 2015	• Serological assays for the determination of antibodies against measles, rubella and varicella viruses will now be performed by a new 3rd party Contract Research Organization (CRO) named NEOMED-LABS Inc. Initially the testing was planned to be performed by GSK Biologicals' laboratory in Rixensart. The assays have been transferred to GSK Biologicals' laboratory in Laval. As of April 1st 2015, the GSK Biologicals' laboratory in Laval became part of Neomed. The only change between GSK Biologicals' laboratory in Laval and NEOMED-LABS Inc. is the name of the laboratory: assays and facilities remain the same. • Due to a delay in the availability of serologic data for the mumps Plaque Reduction Neutralization Test (PRNT) data analysis for this study will be conducted as follows: Part 1 will include a summary of measles, mumps and rubella Enzyme-Linked Immunosorbent Assay (ELISA) results post dose 1 (Day 42) and post dose 2 (Day 84). Part 2 will include a full immunogenicity analysis for post dose 1 (Day 42) and post dose 2 (Day 84) including mumps PRNT results post dose 1, and all safety data.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported