



Clinical trial results:

Efficacy and Safety of a Novel Tetravalent Dengue Vaccine in Healthy Children Aged 2 to 14 Years in Asia

Summary

EudraCT number	2014-001708-24
Trial protocol	Outside EU/EEA
Global end of trial date	21 November 2017

Results information

Result version number	v2 (current)
This version publication date	07 December 2018
First version publication date	17 April 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CYD14
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01373281
WHO universal trial number (UTN)	U1111-1116-4957

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur
Sponsor organisation address	14 Espace Henry Vallée, Lyon, France, 69007
Public contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001201-PIP01-11
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	11 July 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy of CYD dengue vaccine after 3 vaccinations at 0, 6 and 12 months in preventing symptomatic virologically-confirmed dengue cases, regardless of the severity, due to any of the four serotypes in children aged 2 to 14 years at the time of inclusion.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipments were also available on site in case of any immediate allergic reactions.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	03 June 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Philippines: 3501
Country: Number of subjects enrolled	Malaysia: 1401
Country: Number of subjects enrolled	Vietnam: 2333
Country: Number of subjects enrolled	Thailand: 1170
Country: Number of subjects enrolled	Indonesia: 1870
Worldwide total number of subjects	10275
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	7946
Adolescents (12-17 years)	2329
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled from 03 June 2011 to 01 December 2011 at 9 sites in Indonesia, 5 in Malaysia, 3 in Thailand, 5 in Philippines, and 2 in Vietnam.

Pre-assignment

Screening details:

A total of 10275 subjects were enrolled; all but one met all of the inclusion criteria and none of the exclusion criteria. Three subjects were not vaccinated and were excluded from the Full Analysis Set for Efficacy and the Safety Analysis Set.

Period 1

Period 1 title	Vaccination Phase (up to 25 Months)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Blinding implementation details:

An observer-blind procedure was followed for the 3 CYD dengue vaccine or placebo injections. The 'vaccinator' in charge of preparing and administering the vaccines was not authorized to collect safety data and also ensured that the documents on randomization were stored in a secure place with no unauthorized access.

Arms

Are arms mutually exclusive?	Yes
Arm title	CYD Dengue Vaccine Group

Arm description:

Subjects received 3 doses of CYD dengue vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).

Arm type	Experimental
Investigational medicinal product name	CYD dengue vaccine
Investigational medicinal product code	323
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL, subcutaneous, 3 doses at 0, 6, and 12 months.

Arm title	Placebo Group
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Arm description:

Subjects received 3 doses of placebo matched to vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).

Arm type	Placebo
Investigational medicinal product name	Placebo (NaCl)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL, subcutaneous, 3 doses at 0, 6, and 12 months.

Number of subjects in period 1	CYD Dengue Vaccine Group	Placebo Group
Started	6851	3424
Completed	6797	3397
Not completed	54	27
Consent withdrawn by subject	40	23
Serious adverse event	4	1
Lost to follow-up	5	1
Protocol deviation	5	2

Period 2

Period 2 title	Surveillance Expansion Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Blinding implementation details:

An observer-blind procedure was followed for the 3 CYD dengue vaccine or placebo injections. The 'vaccinator' in charge of preparing and administering the vaccines was not authorized to collect safety data and also ensured that the documents on randomization were stored in a secure place with no unauthorized access

Arms

Are arms mutually exclusive?	Yes
Arm title	CYD Dengue Vaccine Group

Arm description:

Subjects received 3 doses of CYD dengue vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).

Arm type	Experimental
Investigational medicinal product name	CYD dengue vaccine
Investigational medicinal product code	323
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL, subcutaneous, 3 doses at 0, 6, and 12 months.

Arm title	Placebo Group
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Arm description:

Subjects received 3 doses of placebo matched to vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).

Arm type	Placebo
Investigational medicinal product name	Placebo (NaCl)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL, subcutaneous, 3 doses at 0, 6, and 12 months.

Number of subjects in period 2	CYD Dengue Vaccine Group	Placebo Group
Started	6797	3397
Completed	6595	3279
Not completed	202	118
Consent withdrawn by subject	180	105
Serious adverse event	3	4
Lost to follow-up	10	8
Protocol deviation	9	1

Baseline characteristics

Reporting groups

Reporting group title	CYD Dengue Vaccine Group
Reporting group description:	
Subjects received 3 doses of CYD dengue vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 3 doses of placebo matched to vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).	

Reporting group values	CYD Dengue Vaccine Group	Placebo Group	Total
Number of subjects	6851	3424	10275
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	5296	2650	7946
Adolescents (12-17 years)	1555	774	2329
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	8.8	8.8	
standard deviation	± 3.45	± 3.42	-
Gender categorical			
Units: Subjects			
Female	3524	1767	5291
Male	3327	1657	4984

End points

End points reporting groups

Reporting group title	CYD Dengue Vaccine Group
Reporting group description: Subjects received 3 doses of CYD dengue vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).	
Reporting group title	Placebo Group
Reporting group description: Subjects received 3 doses of placebo matched to vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).	
Reporting group title	CYD Dengue Vaccine Group
Reporting group description: Subjects received 3 doses of CYD dengue vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).	
Reporting group title	Placebo Group
Reporting group description: Subjects received 3 doses of placebo matched to vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).	

Primary: Number of Symptomatic Virologically Confirmed Dengue (VCD) Cases Due to Any Serotype During the Active Phase Post-Dose 3 Following Injection (Inj.) With Either CYD Dengue Vaccine or a Placebo

End point title	Number of Symptomatic Virologically Confirmed Dengue (VCD) Cases Due to Any Serotype During the Active Phase Post-Dose 3 Following Injection (Inj.) With Either CYD Dengue Vaccine or a Placebo
End point description: Symptomatic VCD cases were defined as occurrence of acute febrile illness (temperature $\geq 38^{\circ}\text{C}$ on at least 2 consecutive days) and confirmation of dengue virus infection by dengue reverse transcriptase polymerase chain reaction (RT-PCR) and/or dengue non-structural protein (NS) 1 antigen enzyme-linked immunosorbent assay (ELISA). Vaccine efficacy was defined as 1 minus the ratio of density incidence due to any serotype after at least 1 dose in the CYD Dengue Vaccine Group over the density incidence of the Placebo Vaccine Group. Number of symptomatic VCD cases were assessed in the Per-Protocol Analysis Set for Efficacy which included subjects who did not meet at least one of the protocol-specified inclusion/exclusion criteria.	
End point type	Primary
End point timeframe: 28 days post-dose 3 and up to 13 months post-dose 3	

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6709	3350		
Units: Cases				
number (not applicable)				
Symptomatic virologically-confirmed dengue cases	117	133		

Statistical analyses

Statistical analysis title	Vaccine efficacy of the CYD dengue vaccine
Statistical analysis description: The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy (expressed in %). The CI was calculated using the exact method conditional on the total number of cases in both groups (exact method by Breslow & Day). The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.	
Comparison groups	CYD Dengue Vaccine Group v Placebo Group
Number of subjects included in analysis	10059
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	56.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	43.8
upper limit	66.4

Secondary: Geometric Mean Titers of Antibodies Against Each Serotype With the Parental Dengue Virus Strain Before and Following Inj. With Either CYD Dengue Tetravalent Vaccine or a Placebo

End point title	Geometric Mean Titers of Antibodies Against Each Serotype With the Parental Dengue Virus Strain Before and Following Inj. With Either CYD Dengue Tetravalent Vaccine or a Placebo
End point description: Geometric mean titers against each of the 4 serotypes of dengue virus strains were assessed using the plaque reduction neutralization test (PRNT) in a pre-defined subset of subjects. Antibody titers against each dengue virus serotype strain were assessed in Full Analysis Set for Immunogenicity (FASI), which included a subset of subjects who received at least one dose of vaccine and had a blood sample drawn and result available after the dose. Here, 'n' = subjects with available data for each specified category.	
End point type	Secondary
End point timeframe: Pre-injection 1, 28 days post Injections 2 and 3, 13 months (Visit 07) and 60 months (Visit 12) post-injection 3	

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1323	660		
Units: Titers 1/Dilution (1/dil)				
geometric mean (confidence interval 95%)				
Dengue virus Serotype 1; Pre-Inj. 1(n=1309,655)	38.3 (33.8 to 43.5)	42.1 (35 to 50.6)		
Dengue virus Serotype 1; Post Inj. 2 (n=1317,654)	153 (137 to 170)	46.1 (38.2 to 55.7)		
Dengue virus Serotype 1; Post Inj. 3 (n=1316,657)	166 (150 to 183)	46.6 (38.7 to 56.1)		
Serotype 1;Year 1 Post Inj.3(V 07) (n=1290,634)	105 (92.8 to 119)	57.2 (46.9 to 69.8)		
Serotype 1; Year 5 Post Inj. 3 (V 12) (n=1275,640)	81.2 (72.5 to 91.0)	77.6 (65.4 to 92.2)		
Dengue virus Serotype 2; Pre-Inj. 1 (n=1313,654)	55.3 (48.7 to 62.9)	62.1 (51.7 to 74.7)		
Dengue virus Serotype 2; Post Inj. 2 (n=1316,655)	360 (329 to 394)	69.5 (57.7 to 83.6)		
Dengue virus Serotype 2; Post Inj. 3 (n=1314, 657)	355 (327 to 386)	68.5 (57.1 to 82.2)		
Serotype 2; Year 1 Post-Inj. 3 (V 07) (n=1298,640)	194 (175 to 214)	78.1 (64.8 to 94.0)		
Serotype 2; Year 5 Post-Inj. 3 (V 12) (n=1275,640)	144 (130 to 160)	102 (86.8 to 120)		
Dengue virus Serotype 3; Pre-Inj. 1 (n=1307,650)	40.1 (35.6 to 45.1)	40.7 (34.5 to 48)		
Dengue virus Serotype 3; Post Inj. 2 (n=1313,656)	203 (184 to 223)	40.8 (34.6 to 48.1)		
Dengue virus Serotype 3; Post Inj. 3 (n=1314,657)	207 (189 to 226)	42.5 (36.2 to 49.9)		
Serotype 3; Year 1 Post Inj. 3 (V 07) (n=1298,639)	186 (168 to 206)	62.1 (51.8 to 74.6)		
Serotype 3; Year 5 Post Inj. 3 (V 12) (n=1275,640)	120 (108 to 133)	76.2 (65.3 to 89.0)		
Dengue virus Serotype 4; Pre Inj. 1 (n=1313,653)	25.3 (22.9 to 28)	26.2 (22.6 to 30.3)		
Dengue virus Serotype 4; Post Inj. 2 (n=1318,655)	151 (139 to 163)	24.4 (21.3 to 28.1)		
Dengue virus Serotype 4; Post Inj. 3 (n=1315,657)	151 (141 to 162)	26 (22.6 to 29.8)		
Serotype 4; Year 1 Post Inj. 3 (V 07) (n=1293,621)	85.5 (78.5 to 93)	26.0 (22.4 to 30.3)		
Serotype 4; Year 5 Post Inj. 3 (V 12) (n=1275,640)	65.7 (60.3 to 71.6)	40.1 (34.8 to 46.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Antibody Titers ≥ 10 1/Dil Against Each Dengue Virus Serotype Strain Before and Following Inj. With CYD Dengue Vaccine or Placebo

End point title	Percentage of Subjects With Antibody Titers ≥ 10 1/Dil Against Each Dengue Virus Serotype Strain Before and
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End point description:

Percentage of subjects with antibody titers ≥ 10 (1/dil) against each serotypes of the dengue virus strains were assessed using PRNT in a pre-defined subset of subjects. Antibody titers against each dengue virus serotype strain were assessed in FASI. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary
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End point timeframe:

Pre-injection 1, 28 days post Injections 2 and 3, 13 months (V 07) and 60 months (V 12) post-injection 3

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1323	660		
Units: Percentage of subjects				
number (not applicable)				
Dengue virus Serotype 1; Pre-Inj. 1 (n=1309,655)	52.0	51.3		
Dengue virus Serotype 1; Post Inj. 2 (n=1317,654)	88.9	54.4		
Dengue virus Serotype 1; Post-Inj. 3 (n=1316,657)	94.0	55.4		
Serotype 1; Year 1 Post-Inj. 3 (V 07) (n=1290,634)	79.8	55.7		
Serotype 1; Year 5 Post-Inj 3 (V 12) (n=1275,640)	76.2	70.0		
Dengue virus Serotype 2; Pre-Inj. 1 (n=1313,654)	58.0	59.3		
Dengue virus Serotype 2; Post-Inj. 2 (n=1316,655)	97.3	62.4		
Dengue virus Serotype 2; Post-Inj. 3 (n=1314,657)	98.7	61.8		
Serotype 2; Year 1 Post-Inj. 3 (V 07) (n=1298,640)	92.0	65.8		
Serotype 2; Year 5 Post-inj 3 (V 12) (n=1275,640)	86.0	75.2		
Dengue virus Serotype 3; Pre-Inj. 1 (n=1307,650)	56.8	59.4		
Dengue virus Serotype 3; Post-Inj. 2 (n=1313,656)	95.7	60.2		
Dengue virus Serotype 3; Post-Inj. 3 (n=1314,657)	97.0	61.0		
Serotype 3; Year 1 Post-Inj. 3 (V 07) (n=1298,639)	93.6	62.6		
Serotype 3; Year5 Post-Inj. 3 (V 12) (n=1275,640)	87.4	75.6		
Dengue virus Serotype 4; Pre-Inj. 1 (n=1313,653)	51.6	50.7		
Dengue virus Serotype 4; Post-Inj. 2 (n=1318,655)	95.1	51.8		
Dengue virus Serotype 4; Post-Inj. 3 (n=1315,657)	97.0	53.9		
Serotype 4; Year 1 Post-Inj 3 (V 07) (n=1293,621)	89.4	50.6		
Serotype 4; Year 5 Post-Inj 3 (V 12) (n=1275,640)	83.8	65.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Solicited Injection Site Reactions Following Any and Each Inj. With Either CYD Dengue Vaccine or a Placebo

End point title	Number of Subjects With Solicited Injection Site Reactions Following Any and Each Inj. With Either CYD Dengue Vaccine or a Placebo
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End point description:

Solicited injection site reactions: Pain, Erythema, and Swelling. Grade 3 reactions (2-11 years) - Pain: incapacitating, unable to perform usual activities; Erythema and Swelling, ≥ 50 mm. Grade 3 Solicited injection site reactions (12-14 years): Pain, Significant, prevents daily activity; Erythema and Swelling, >100 mm. Solicited injection site reactions were assessed in a subset of the Safety Analysis Set, which included all subjects who received at least one dose of study vaccine. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary
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End point timeframe:

Within 7 days after injection

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1334	663		
Units: Number of subjects				
number (not applicable)				
Inj. site Pain (Post any Inj.) (n=1332,663)	614	275		
Inj. site Erythema (Post-any Inj.) (n=1332,663)	107	52		
Inj. site Swelling (Post any Inj.) (n=1332,663)	68	33		
Inj. site Pain (Post-Inj. 1) (n=1332,663)	406	196		
Grade 3 Inj. site Pain (Post- Inj. 1)(n=1332,663)	1	0		
Inj. site Erythema (Post Inj. 1) (n=1332,663)	63	35		
Grade 3 Inj. site Erythema(Post Inj.1)(n=1332,663)	0	0		
Inj. site Swelling (Post Inj.1)(n=1332,663)	40	19		
Grade 3 Inj. site Swelling(Post Inj.1)(n=1332,663)	0	0		
Inj. site Pain (Post Inj.2)(n=1319,658)	303	135		
Grade 3 Inj. site Pain (Post- Inj.2)(n=1319,658)	0	0		
Inj. site Erythema (Post Inj.2)(n=1319,658)	43	20		

Grade 3 Inj. site Erythema(Post Inj.2)(n=1319,658)	0	0		
Inj. site Swelling (Post Inj.2)(n=1319,658)	25	7		
Grade 3 Inj. site Swelling(Post Inj.2)(n=1319,658)	0	0		
Inj. site Pain (Post Inj. 3)(n=1313,654)	283	118		
Grade 3 Inj. site Pain (Post Inj. 3)(n=1313,654)	0	0		
Inj. site Erythema (Post Inj.3)(n=1313,654)	36	16		
Grade 3 Inj. site Erythema(Post Inj.3)(n=1313,654)	0	1		
Inj. site Swelling (Post Inj.3)(n=1313,654)	19	10		
Grade 3 Inj. site Swelling(Post Inj.3)(n=1313,654)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Symptomatic VCD Cases Due to Any Serotype Occurring 28 Days Post-Dose 1 Following Inj. With Either CYD Dengue Vaccine or a Placebo

End point title	Number of Symptomatic VCD Cases Due to Any Serotype Occurring 28 Days Post-Dose 1 Following Inj. With Either CYD Dengue Vaccine or a Placebo
End point description:	Symptomatic VCD cases were defined as occurrence of acute febrile illness (temperature $\geq 38^{\circ}\text{C}$ on at least 2 consecutive days) and confirmation of dengue virus infection by dengue RT-PCR and/or dengue NS1 ELISA. Vaccine efficacy was defined as 1 minus the ratio of density incidence due to any serotype after at least 1 dose in the CYD Dengue Vaccine Group over the density incidence of the Placebo Vaccine Group. Number of symptomatic VCD cases were assessed in the Full Analysis Set for Efficacy, which included subjects who received at least 1 dose of study vaccine.
End point type	Secondary
End point timeframe:	28 days post-injection 1 and up to 13 months post-injection 3

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6848	3424		
Units: Cases				
number (not applicable)	276	302		

Statistical analyses

Statistical analysis title	CYD Dengue Vaccine Group, Placebo Group
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Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% CI of the vaccine efficacy (expressed in %) calculated using the exact method conditional on the total number of cases in both groups.

Comparison groups	CYD Dengue Vaccine Group v Placebo Group
Number of subjects included in analysis	10272
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine Efficacy
Point estimate	55.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	47.3
upper limit	62.3

Secondary: Number of Symptomatic VCD Cases Meeting 1997 World Health Organization (WHO) Criteria During the Surveillance Expansion Period Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo

End point title	Number of Symptomatic VCD Cases Meeting 1997 World Health Organization (WHO) Criteria During the Surveillance Expansion Period Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo
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End point description:

The 1997 WHO criteria are: a) Fever: acute onset, high ($\geq 38^{\circ}\text{C}$) and continuous, for 2 to 7 days and (b) any of the following: thrombocytopenia (platelet $\leq 100 \times 10^9/\text{L}$) and plasma leakage as shown by hematocrit increased by 20% or more or pleural effusion and/or ascites and/or hypoalbuminemia. The first two clinical criteria plus thrombocytopenia and signs of plasma leakage are enough to establish diagnosis of Dengue hemorrhagic fever (DHF). DHF was graded as follows: Grade I: Fever accompanied by non-specific constitutional symptoms; the only hemorrhagic manifestation is a positive tourniquet test; Grade II: Spontaneous bleeding in addition to the manifestations of Grade I subjects, usually in the form of skin and/or other hemorrhages; Grade III: Circulatory failure manifested by rapid and weak pulse, narrowing of pulse pressure (20mmHg or less) or hypotension, with the presence of cold clammy skin and restlessness; and Grade IV: Profound shock with undetectable blood pressure and pulse.

End point type	Secondary
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End point timeframe:

From consent to participate in Surveillance Expansion Period to 60 months post-injection 3 (up to Month 72)

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6327	3138		
Units: Cases				
number (not applicable)				
Due to Any of the 4 Serotypes: Any Grade	19	12		
Due to Any of the 4 Serotypes: Grade I	5	3		
Due to Any of the 4 Serotypes: Grade II	11	8		
Due to Any of the 4 Serotypes: Grade III	3	1		

Due to Any of the 4 Serotypes: Grade IV	0	0		
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of Clinically Severe VCD Cases During the Surveillance Expansion Period Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo

End point title	Number of Clinically Severe VCD Cases During the Surveillance Expansion Period Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo
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End point description:

The severity of VCD cases was assessed by an IDMC based on a medical review of cases and any of the following criteria: 1) Platelet count $\leq 100000/\mu\text{L}$ and bleeding (tourniquet, petechiae or any bleeding) plus plasma leakage 2) Shock (pulse pressure $\leq 20\text{ mmHg}$ in a child, or hypotension [$\leq 90\text{ mmHg}$] with tachycardia, weak pulse and poor perfusion) 3) Bleeding requiring blood transfusion 4) Encephalopathy i.e. Unconsciousness or poor conscious state or fitting not attributable to simple febrile convulsion or focal neurological signs. Poor conscious state or unconsciousness must be supported by Glasgow Coma Scale (GCS) score. 5) Liver impairment (AST 1000 IU/L or prothrombin time [PT] International normalized ratio [INR] > 1.5) excluding other causes of viral hepatitis 6) Impaired kidney function (serum creatinine $\geq 1.5\text{ mg/dL}$) 7) Myocarditis, pericarditis or clinical heart failure supported by Chest X-Ray (CXR), echocardiography, electrocardiogram (ECG) or cardiac enzymes. Full Analysis Set for SEP.

End point type	Secondary
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End point timeframe:

From consent to participate in the Surveillance Expansion Period to 60 months post-injection 3 (up to Month 72)

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6327	3138		
Units: Cases				
number (not applicable)	21	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Symptomatic VCD Cases Due to Any Serotype 28 Days Post-Dose 2 Following Inj. With Either CYD Dengue Vaccine or a Placebo

End point title	Number of Symptomatic VCD Cases Due to Any Serotype 28 Days Post-Dose 2 Following Inj. With Either CYD Dengue Vaccine or a Placebo
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End point description:

Symptomatic VCD cases were defined as occurrence of acute febrile illness (temperature $\geq 38^\circ\text{C}$ on at least 2 consecutive days) and confirmation of dengue virus infection by dengue RT-PCR and/or dengue

NS1 ELISA. Vaccine efficacy was defined as 1 minus the ratio of density incidence due to any serotype after at least 1 dose in the CYD Dengue Vaccine Group over the density incidence of the Placebo Vaccine Group. Number of symptomatic VCD cases were assessed in the Other Efficacy Analysis Set, which included subjects who received at least 2 doses of study vaccine.

End point type	Secondary
End point timeframe:	
28 days post-injection 2 and up to 13 months post-injection 3	

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6793	3397		
Units: Cases				
number (not applicable)	205	238		

Statistical analyses

Statistical analysis title	CYD Dengue Vaccine Group, Placebo Group
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Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% CI of the vaccine efficacy (expressed in %) calculated using the exact method conditional on the total number of cases in both groups.

Comparison groups	CYD Dengue Vaccine Group v Placebo Group
Number of subjects included in analysis	10190
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine Efficacy
Point estimate	57.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	49
upper limit	65.2

Secondary: Number of Symptomatic VCD Cases Due to Any Serotype During the Active Phase in Either CYD Dengue Vaccine or Placebo Group

End point title	Number of Symptomatic VCD Cases Due to Any Serotype During the Active Phase in Either CYD Dengue Vaccine or Placebo Group
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End point description:

Symptomatic VCD cases were defined as occurrence of acute febrile illness (temperature $\geq 38^{\circ}\text{C}$ on at least 2 consecutive days) and confirmation of dengue virus infection by dengue RT-PCR and/or dengue NS1 ELISA. Vaccine efficacy was defined as 1 minus the ratio of density incidence due to any serotype after at least 1 dose in the CYD Dengue Vaccine Group over the density incidence of the Placebo Vaccine Group. Number of symptomatic VCD cases were assessed in the Full Analysis Set for Efficacy, which included all subjects who received at least 1 injection.

End point type	Secondary
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End point timeframe:

Day 0 up to 13 months post-injection 3

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6848	3424		
Units: Cases				
number (not applicable)	286	309		

Statistical analyses

Statistical analysis title	CYD Dengue Vaccine Group, Placebo Group
Statistical analysis description: The statistical methodology was based on the use of the two-sided 95% CI of the vaccine efficacy (expressed in %) calculated using the exact method conditional on the total number of cases in both groups.	
Comparison groups	CYD Dengue Vaccine Group v Placebo Group
Number of subjects included in analysis	10272
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine Efficacy
Point estimate	54.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	46.8
upper limit	61.7

Secondary: Number of Clinically Severe VCD Cases Throughout the Trial Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo

End point title	Number of Clinically Severe VCD Cases Throughout the Trial Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo
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End point description:

The severity of VCD cases was assessed by an IDMC based on a medical review of cases and any of the following criteria: 1) Platelet count $\leq 100000\mu\text{l}$ and bleeding (tourniquet, petechiae or any bleeding) plus plasma leakage 2) Shock (pulse pressure $\leq 20\text{mmHg}$ in a child, or hypotension [$\leq 90\text{ mmHg}$] with tachycardia, weak pulse and poor perfusion) 3) Bleeding requiring blood transfusion 4) Encephalopathy i.e. Unconsciousness or poor conscious state or fitting not attributable to simple febrile convulsion or focal neurological signs. Poor conscious state or unconsciousness must be supported by GCS score. 5) Liver impairment (AST $>1000\text{IU/L}$ or PT International normalized ratio [INR] >1.5) excluding other causes of viral hepatitis 6) Impaired kidney function (serum creatinine $\geq 1.5\text{mg/dL}$) 7) Myocarditis, pericarditis or clinical heart failure supported by CXR, echocardiography, ECG or cardiac enzymes. Number of clinically severe VCD cases were assessed in the Safety Analysis Set.

End point type	Secondary
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End point timeframe:

Day 0 to the end of study (up to 72 months)

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6745	3369		
Units: Cases				
number (not applicable)	61	41		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Systemic Reactions Following Any and Each Inj. With Either CYD Dengue Vaccine or a Placebo

End point title	Number of Subjects With Systemic Reactions Following Any and Each Inj. With Either CYD Dengue Vaccine or a Placebo
End point description:	
Solicited systemic reactions: Fever (Temperature), Headache, Malaise, Myalgia, and Asthenia. Grade 3 reactions- Fever: $\geq 39^{\circ}\text{C}$; Headache, Malaise, Myalgia, and Asthenia, Significant, prevents daily activity. Solicited systemic reactions were assessed in a subset of the Safety Analysis Set, which included all subjects who received at least one dose of study vaccine. Here, 'n' = subjects with available data for each specified category.	
End point type	Secondary
End point timeframe:	
Within 14 days after injection	

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1334	663		
Units: Number of subjects				
number (not applicable)				
Fever (Post any injection) (n=1332,663)	248	118		
Headache (Post any injection) (n=1332,663)	562	259		
Malaise (Post any injection) (n=1332,663)	476	239		
Myalgia (Post any injection) (n=1332,663)	414	197		
Asthenia (Post any injection) (n=1332,663)	378	167		
Fever (Post-injection 1) (n=1330,663)	103	45		
Grade 3 Fever (Post-injection 1) (n=1330,663)	18	7		
Headache (Post-injection 1) (n=1332,663)	387	168		
Grade 3 Headache (Post-injection 1) (n=1332,663)	7	6		

Malaise (Post-injection 1) (n=1332,663)	312	148		
Grade 3 Malaise (Post-injection 1) (n=1332,663)	7	4		
Myalgia (Post-injection 1) (n=1332,663)	255	124		
Grade 3 Myalgia (Post-injection 1) (n=1332,663)	2	2		
Asthenia (Post-injection 1) (n=1332,663)	229	97		
Grade 3 Asthenia (Post-injection 1) (n=1332,663)	5	5		
Fever (Post-injection 2) (n=1320,657)	90	44		
Grade 3 Fever (Post-injection 2) (n=1320,657)	19	9		
Headache (Post-injection 2) (n=1319,658)	247	118		
Grade 3 Headache (Post-injection 2) (n=1319,658)	12	3		
Malaise (Post-injection 2) (n=1319,658)	192	100		
Grade 3 Malaise (Post-injection 2) (n=1319,658)	6	4		
Myalgia (Post-injection 2) (n=1319,658)	174	92		
Grade 3 Myalgia (Post-injection 2) (n=1319,658)	3	0		
Asthenia (Post-injection 2) (n=1319,658)	158	74		
Grade 3 Asthenia (Post-injection 2) (n=1319,658)	5	6		
Fever (Post-injection 3) (n=1309,654)	76	39		
Grade 3 Fever (Post-injection 3) (n=1309,654)	16	2		
Headache (Post-injection 3) (n=1313,654)	219	113		
Grade 3 Headache (Post-injection 3) (n=1313,654)	6	1		
Malaise (Post-injection 3) (n=1313,654)	183	104		
Grade 3 Malaise (Post-injection 3) (n=1313,654)	7	1		
Myalgia (Post-injection 3) (n=1313,654)	156	76		
Grade 3 Myalgia (Post-injection 3) (n=1313,654)	3	0		
Asthenia (Post-injection 3) (n=1313,654)	142	73		
Grade 3 Asthenia (Post-injection 3) (n=1313,654)	4	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Hospitalized VCD Cases During the Surveillance Expansion Period Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo

End point title	Number of Hospitalized VCD Cases During the Surveillance Expansion Period Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo
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End point description:

Hospitalized VCD cases were defined as VCD confirmed by dengue RT –PCR and/or dengue NS1 ELISA in subjects with acute febrile illness (temperature $\geq 38^{\circ}\text{C}$ on at least 2 consecutive days) requiring hospitalization.

Number of hospitalized VCD cases were assessed in the Safety Analysis Set.

End point type	Secondary
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End point timeframe:

From consent to participate in the Surveillance Expansion Period to 60 months post-injection 3 (up to Month 72)

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6848	3424		
Units: Cases				
number (not applicable)	74	48		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Hospitalized VCD Cases Throughout the Trial Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo

End point title	Number of Hospitalized VCD Cases Throughout the Trial Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo
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End point description:

Hospitalized VCD cases were defined as VCD confirmed by dengue RT –PCR and/or dengue NS1 ELISA in subjects with acute febrile illness (temperature $\geq 38^{\circ}\text{C}$ on at least 2 consecutive days) requiring hospitalization.

Number of VCD cases were assessed in the Safety Analysis Set.

End point type	Secondary
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End point timeframe:

Day 0 to the end of study (up to 72 months)

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6745	3369		
Units: Cases				
number (not applicable)	210	154		

Statistical analyses

Secondary: Number of Symptomatic VCD Cases Meeting 1997 WHO Criteria Throughout the Trial Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo

End point title	Number of Symptomatic VCD Cases Meeting 1997 WHO Criteria Throughout the Trial Due to Any Serotype Following Inj. With Either CYD Dengue Vaccine or a Placebo
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End point description:

The 1997 WHO criteria are: a) Fever: acute onset, high ($\geq 38^{\circ}\text{C}$) and continuous, for 2 to 7 days and (b) any of the following: thrombocytopenia (platelet $\leq 100 \times 10^9/\text{L}$) and plasma leakage as shown by hematocrit increased by 20% or more or pleural effusion and/or ascites and/or hypoalbuminemia. The first two clinical criteria plus thrombocytopenia and signs of plasma leakage are enough to establish diagnosis of DHF. DHF was graded as follows: Grade I: Fever accompanied by non-specific constitutional symptoms; the only hemorrhagic manifestation is a positive tourniquet test; Grade II: Spontaneous bleeding in addition to the manifestations of Grade I subjects, usually in the form of skin and/or other hemorrhages; Grade III: Circulatory failure manifested by rapid and weak pulse, narrowing of pulse pressure (20 mmHg or less) or hypotension, with the presence of cold clammy skin and restlessness; and Grade IV: Profound shock with undetectable blood pressure and pulse. Full Analysis Set for SEP.

End point type	Secondary
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End point timeframe:

Day 0 to the end of study (up to 72 months)

End point values	CYD Dengue Vaccine Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6745	3369		
Units: Cases				
number (not applicable)				
Due to Any of the 4 Serotypes: Any Grade	55	41		
Due to Any of the 4 Serotypes: Grade I	14	9		
Due to Any of the 4 Serotypes: Grade II	37	29		
Due to Any of the 4 Serotypes: Grade III	4	3		
Due to Any of the 4 Serotypes: Grade IV	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE data were collected from Day 0 (post-vaccination) up to 60 months post-injection 3 (up to 72 months).

Adverse event reporting additional description:

All vaccinated subjects were assessed for serious AEs during the trial. Non-serious AEs were assessed in a subset of subjects from each group, and included solicited injection site and systemic reactions (within 7 and 14 days after injection), as well as unsolicited non-serious AEs (28 days after injection).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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Reporting groups

Reporting group title	CYD Dengue Vaccine Group
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Reporting group description:

Subjects received 3 doses of CYD dengue vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).

Reporting group title	Placebo Group
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Reporting group description:

Subjects received 3 doses of placebo matched to vaccine; one each at 0, 6, and 12 months and were followed up to 60 months after last vaccination (for a total duration of up to 72 months).

Serious adverse events	CYD Dengue Vaccine Group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	947 / 6848 (13.83%)	552 / 3424 (16.12%)	
number of deaths (all causes)	10	4	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute Lymphocytic Leukaemia			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angiofibroma			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign Neoplasm Of Skin			

subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign Soft Tissue Neoplasm			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone Giant Cell Tumour Benign			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone Sarcoma			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Neoplasm			
subjects affected / exposed	3 / 6848 (0.04%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear Neoplasm			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibroadenoma Of Breast			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibrous Histiocytoma			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemangioma			

subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip Neoplasm Benign			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipoma			
subjects affected / exposed	0 / 6848 (0.00%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangioma			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Papilloma			
subjects affected / exposed	0 / 6848 (0.00%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft Tissue Neoplasm			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Teratoma			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aneurysm Ruptured			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematoma			

subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Abortion Induced			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion Complete			
subjects affected / exposed	3 / 6848 (0.04%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion Incomplete			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion Spontaneous			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion Spontaneous Incomplete			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion Threatened			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Breech Presentation			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cephalo-Pelvic Disproportion			
subjects affected / exposed	3 / 6848 (0.04%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eclampsia			
subjects affected / exposed	3 / 6848 (0.04%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ectopic Pregnancy			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
False Labour			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal Distress Syndrome			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oligohydramnios			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postpartum Haemorrhage			
subjects affected / exposed	0 / 6848 (0.00%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature Labour			

subjects affected / exposed	4 / 6848 (0.06%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Puerperal Pyrexia			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stillbirth			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Drowning			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hernia Obstructive			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergy To Arthropod Bite			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Allergy To Arthropod Sting			
subjects affected / exposed	4 / 6848 (0.06%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Anaphylactic Reaction			
subjects affected / exposed	3 / 6848 (0.04%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic Shock			
subjects affected / exposed	1 / 6848 (0.01%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug Hypersensitivity			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food Allergy			
subjects affected / exposed	5 / 6848 (0.07%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	2 / 6848 (0.03%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Child Abuse			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Physical Assault			
subjects affected / exposed	4 / 6848 (0.06%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Victim Of Child Abuse			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Victim Of Crime			

subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Victim Of Sexual Abuse			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Acquired Phimosi			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast Mass			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysfunctional Uterine Bleeding			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometriosis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic Ovarian Cyst			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian Cyst			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian Haemorrhage			

subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine Cervical Erosion			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine Haemorrhage			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal Haematoma			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Adenoidal Hypertrophy			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asphyxia			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	12 / 6848 (0.18%)	9 / 3424 (0.26%)	
occurrences causally related to treatment / all	0 / 19	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial Hyperreactivity			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal Polyps			

subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal Septum Deviation			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neonatal Asphyxia			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Acidosis			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Inflammation			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Abnormal Behaviour			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Psychosis			

subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar I Disorder			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar Disorder			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental Disorder			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychosomatic Disease			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic Disorder			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatoform Disorder			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide Attempt			

subjects affected / exposed	1 / 6848 (0.01%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	4 / 6848 (0.06%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adverse Event Following Immunisation			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Animal Bite			
subjects affected / exposed	2 / 6848 (0.03%)	4 / 3424 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropod Bite			
subjects affected / exposed	3 / 6848 (0.04%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns Second Degree			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chemical Poisoning			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chest Injury			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle Fracture			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	7 / 6848 (0.10%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear Injury			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrical Burn			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Excoriation			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye Injury			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyeball Rupture			

subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial Bones Fracture			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	15 / 6848 (0.22%)	6 / 3424 (0.18%)	
occurrences causally related to treatment / all	0 / 16	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur Fracture			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula Fracture			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot Fracture			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm Fracture			
subjects affected / exposed	9 / 6848 (0.13%)	4 / 3424 (0.12%)	
occurrences causally related to treatment / all	0 / 9	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign Body			
subjects affected / exposed	5 / 6848 (0.07%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign Body In Eye			

subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital Injury			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gun Shot Wound			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand Fracture			
subjects affected / exposed	3 / 6848 (0.04%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head Injury			
subjects affected / exposed	5 / 6848 (0.07%)	4 / 3424 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus Fracture			
subjects affected / exposed	9 / 6848 (0.13%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 9	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impacted Fracture			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	1 / 6848 (0.01%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional Overdose			

subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Dislocation			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Injury			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament Sprain			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb Injury			
subjects affected / exposed	1 / 6848 (0.01%)	3 / 3424 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Limb Fracture			
subjects affected / exposed	1 / 6848 (0.01%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Fractures			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Injuries			

subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle Strain			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Near Drowning			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open Wound			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Poisoning Deliberate			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Adhesion			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Ileus			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius Fracture			

subjects affected / exposed	6 / 6848 (0.09%)	5 / 3424 (0.15%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road Traffic Accident			
subjects affected / exposed	71 / 6848 (1.04%)	38 / 3424 (1.11%)	
occurrences causally related to treatment / all	0 / 75	0 / 39	
deaths causally related to treatment / all	0 / 6	0 / 0	
Scrotal Haematoma			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Snake Bite			
subjects affected / exposed	4 / 6848 (0.06%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft Tissue Injury			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sports Injury			
subjects affected / exposed	5 / 6848 (0.07%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stab Wound			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon Rupture			
subjects affected / exposed	3 / 6848 (0.04%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal Burn			

subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia Fracture			
subjects affected / exposed	1 / 6848 (0.01%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity To Various Agents			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal Injury			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Traumatic Brain Injury			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic Intracranial Haemorrhage			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Limb Fracture			
subjects affected / exposed	3 / 6848 (0.04%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duchenne Muscular Dystrophy			

subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Familial Periodic Paralysis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibrous Dysplasia Of Bone			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Odontogenic Cyst			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phimosis			
subjects affected / exposed	0 / 6848 (0.00%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac Failure Congestive			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic Shock			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rheumatic Heart Disease			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular Tachycardia			

subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular Tachycardia			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Acute Disseminated Encephalomyelitis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autonomic Neuropathy			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral Venous Thrombosis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complex Partial Seizures			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	4 / 6848 (0.06%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsions Local			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			

subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epilepsy			
subjects affected / exposed	8 / 6848 (0.12%)	4 / 3424 (0.12%)	
occurrences causally related to treatment / all	0 / 9	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extrapyramidal Disorder			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile Convulsion			
subjects affected / exposed	13 / 6848 (0.19%)	7 / 3424 (0.20%)	
occurrences causally related to treatment / all	0 / 23	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Grand Mal Convulsion			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre Syndrome			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intercostal Neuralgia			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic Stroke			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine Without Aura			

subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial Seizures			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status Epilepticus			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension Headache			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonic Convulsion			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viith Nerve Paralysis			
subjects affected / exposed	3 / 6848 (0.04%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia Of Pregnancy			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic Anaemia			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron Deficiency Anaemia			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Middle Ear Effusion			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo Positional			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular Disorder			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Chalazion			
subjects affected / exposed	3 / 6848 (0.04%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choroidal Dystrophy			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal Oedema			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain Lower			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain Upper			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Fistula			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Caecitis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			

subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental Caries			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	6 / 6848 (0.09%)	6 / 3424 (0.18%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	8 / 6848 (0.12%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	5 / 6848 (0.07%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food Poisoning			
subjects affected / exposed	9 / 6848 (0.13%)	3 / 3424 (0.09%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	31 / 6848 (0.45%)	14 / 3424 (0.41%)	
occurrences causally related to treatment / all	0 / 32	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Disorder			

subjects affected / exposed	9 / 6848 (0.13%)	5 / 3424 (0.15%)	
occurrences causally related to treatment / all	0 / 10	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Inflammation			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal Hernia			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth Cyst			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis Acute			

subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis Chronic			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontitis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary Gland Calculus			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary Gland Mucocoele			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth Development Disorder			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth Impacted			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toothache			

subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermal Cyst			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Henoch-Schonlein Purpura			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Hypertrophy			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 6848 (0.01%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus Ureteric			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis Acute			
subjects affected / exposed	3 / 6848 (0.04%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic Syndrome			

subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurogenic Bladder			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post Streptococcal Glomerulonephritis			
subjects affected / exposed	9 / 6848 (0.13%)	3 / 3424 (0.09%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Failure Acute			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Tubular Acidosis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone Cyst			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exostosis			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fasciitis			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture Malunion			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw Cyst			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle Spasms			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatic Fever			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial Cyst			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Abscess Limb			
subjects affected / exposed	4 / 6848 (0.06%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess Neck			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess Of External Auditory Meatus			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acinetobacter Bacteraemia			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Sinusitis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Tonsillitis			
subjects affected / exposed	7 / 6848 (0.10%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoiditis			
subjects affected / exposed	4 / 6848 (0.06%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amoebiasis			
subjects affected / exposed	9 / 6848 (0.13%)	4 / 3424 (0.12%)	
occurrences causally related to treatment / all	0 / 9	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amoebic Dysentery			

subjects affected / exposed	3 / 6848 (0.04%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Abscess			
subjects affected / exposed	0 / 6848 (0.00%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendiceal Abscess			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	33 / 6848 (0.48%)	27 / 3424 (0.79%)	
occurrences causally related to treatment / all	0 / 33	0 / 27	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis Perforated			
subjects affected / exposed	5 / 6848 (0.07%)	4 / 3424 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial Diarrhoea			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial Infection			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bartholin's Abscess			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			

subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	16 / 6848 (0.23%)	6 / 3424 (0.18%)	
occurrences causally related to treatment / all	0 / 16	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis Bacterial			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	8 / 6848 (0.12%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brucellosis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	7 / 6848 (0.10%)	3 / 3424 (0.09%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chikungunya Virus Infection			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Tonsillitis			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis Infective			

subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	3 / 6848 (0.04%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue Fever			
subjects affected / exposed	238 / 6848 (3.48%)	158 / 3424 (4.61%)	
occurrences causally related to treatment / all	0 / 241	0 / 167	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea Infectious			
subjects affected / exposed	3 / 6848 (0.04%)	5 / 3424 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated Tuberculosis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis Viral			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Furuncle			
subjects affected / exposed	3 / 6848 (0.04%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis Bacterial			

subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	53 / 6848 (0.77%)	40 / 3424 (1.17%)	
occurrences causally related to treatment / all	0 / 64	0 / 43	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Bacterial			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Viral			
subjects affected / exposed	3 / 6848 (0.04%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Bacterial Infection			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Infection			
subjects affected / exposed	6 / 6848 (0.09%)	5 / 3424 (0.15%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin Abscess			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiv Infection			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-Foot-And-Mouth Disease			

subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis Viral			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpangina			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes Zoster			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hordeolum			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection In An Immunocompromised Host			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	9 / 6848 (0.13%)	3 / 3424 (0.09%)	
occurrences causally related to treatment / all	0 / 9	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leptospirosis			

subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar Pneumonia			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis Bacterial			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaria			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Measles			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis Aseptic			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis Bacterial			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mumps			

subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral Herpes			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis Externa			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis Media			
subjects affected / exposed	2 / 6848 (0.03%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis Media Chronic			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paratyphoid Fever			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			

subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital Cellulitis			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar Abscess			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	32 / 6848 (0.47%)	19 / 3424 (0.55%)	
occurrences causally related to treatment / all	0 / 35	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis Bacterial			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis Streptococcal			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	15 / 6848 (0.22%)	4 / 3424 (0.12%)	
occurrences causally related to treatment / all	0 / 15	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmodium Falciparum Infection			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	33 / 6848 (0.48%)	12 / 3424 (0.35%)	
occurrences causally related to treatment / all	0 / 37	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Bacterial			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Measles			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Primary Atypical			
subjects affected / exposed	2 / 6848 (0.03%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Viral			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Wound Infection			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Tuberculosis			
subjects affected / exposed	5 / 6848 (0.07%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis Acute			

subjects affected / exposed	4 / 6848 (0.06%)	3 / 3424 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Tract Infection			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scarlet Fever			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 6848 (0.03%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sinusitis			
subjects affected / exposed	4 / 6848 (0.06%)	2 / 3424 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal Sepsis			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal Infection			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	12 / 6848 (0.18%)	4 / 3424 (0.12%)	
occurrences causally related to treatment / all	0 / 12	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis Bacterial			

subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth Abscess			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculous Pleurisy			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Typhoid Fever			
subjects affected / exposed	15 / 6848 (0.22%)	13 / 3424 (0.38%)	
occurrences causally related to treatment / all	0 / 18	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Typhus			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	11 / 6848 (0.16%)	5 / 3424 (0.15%)	
occurrences causally related to treatment / all	0 / 11	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethritis			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			

subjects affected / exposed	22 / 6848 (0.32%)	14 / 3424 (0.41%)	
occurrences causally related to treatment / all	0 / 23	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Infection			
subjects affected / exposed	32 / 6848 (0.47%)	29 / 3424 (0.85%)	
occurrences causally related to treatment / all	0 / 35	0 / 29	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Pharyngitis			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Rash			
subjects affected / exposed	0 / 6848 (0.00%)	3 / 3424 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval Abscess			
subjects affected / exposed	1 / 6848 (0.01%)	0 / 3424 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound Infection			
subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Calcium Deficiency			

subjects affected / exposed	1 / 6848 (0.01%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	0 / 6848 (0.00%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	2 / 6848 (0.03%)	1 / 3424 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CYD Dengue Vaccine Group	Placebo Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	942 / 6848 (13.76%)	453 / 3424 (13.23%)	
Nervous system disorders			
Headache			
subjects affected / exposed ^[1]	567 / 1334 (42.50%)	264 / 663 (39.82%)	
occurrences (all)	866	409	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed ^[2]	378 / 1334 (28.34%)	167 / 663 (25.19%)	
occurrences (all)	530	244	
Injection Site Erythema			
subjects affected / exposed ^[3]	107 / 1334 (8.02%)	52 / 663 (7.84%)	
occurrences (all)	142	71	
Injection Site Pain			

subjects affected / exposed ^[4]	616 / 1334 (46.18%)	275 / 663 (41.48%)	
occurrences (all)	994	449	
Injection Site Swelling			
subjects affected / exposed ^[5]	68 / 1334 (5.10%)	33 / 663 (4.98%)	
occurrences (all)	84	36	
Malaise			
subjects affected / exposed ^[6]	476 / 1334 (35.68%)	239 / 663 (36.05%)	
occurrences (all)	689	352	
Pyrexia			
subjects affected / exposed ^[7]	267 / 1334 (20.01%)	125 / 663 (18.85%)	
occurrences (all)	291	137	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed ^[8]	63 / 1334 (4.72%)	48 / 663 (7.24%)	
occurrences (all)	69	61	
Rhinorrhoea			
subjects affected / exposed ^[9]	46 / 1334 (3.45%)	36 / 663 (5.43%)	
occurrences (all)	48	43	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed ^[10]	414 / 1334 (31.03%)	197 / 663 (29.71%)	
occurrences (all)	585	296	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed ^[11]	85 / 1334 (6.37%)	45 / 663 (6.79%)	
occurrences (all)	113	61	
Upper Respiratory Tract Infection			
subjects affected / exposed ^[12]	95 / 1334 (7.12%)	54 / 663 (8.14%)	
occurrences (all)	104	62	

Notes:

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

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

Justification: Non-serious adverse events were assessed in a subset of subjects in each group, in accordance with the protocol.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 January 2011	The 'Other Objectives' section was revised to improve specificity of confirmation of dengue in line with the non-primary endpoint suggested in the WHO guidelines (version 2.0); It was also specified that the safety surveillance will be conducted by the Principal Investigators.
03 August 2011	Clarified the issue of sample collection times and the reporting period; Extended the collection of all SAEs to the entire study period; Noted that laboratory staff is blinded to treatment allocation and also the stratification by age as (2 to 5 years, 6 to 11 years, and 12 to 14 years); and updated the time window for assessment of serious viscerotropic disease in-line with the update of the Guidelines for Assessing Viscerotropic and Neurotropic Adverse Events, and introduced the use of the WHO Verbal Autopsy Questionnaire.
29 May 2013	Modified the testing algorithm for the virological-confirmation by adding the dengue screen RT-PCR and the Simplexa RT-PCR, assessment of the CYD dengue vaccine in preventing symptomatic virologically-confirmed dengue cases; The study objectives was revised along with the addition of 'Other Objectives'; The Hospital Phase was extended by 2 years to allow a 5-year follow-up period after the last vaccination; and the addition of use of neutralization antibody assays and analyses in addition to PRNT to characterize the immune response.
25 January 2015	Enhanced the surveillance system also known as the Surveillance Expansion Phase (SEP). The subjects who consented to SEP were actively followed for dengue case detection, and an additional visit (Vse) and blood sample at SEP requested. The trial objectives were modified to add other objectives and endpoints; to describe the occurrence of hospitalized VCD cases and severe VCD throughout SEP and entire trial duration and correlate immunogenicity profile as assessed by PRNT at post-dose 3 and/or at the time of SEP enrollment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25018116>

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