Clinical trial results:
A Study of Dengue Vaccine in Healthy Toddlers Aged 12 to 15 Months in the Philippines

Summary

EudraCT number	2014-001694-14
Trial protocol	Outside EU/EEA
Global end of trial date	08 May 2012

Results information

Result version number	v1 (current)
This version publication date	16 February 2016
First version publication date	31 July 2015

Trial information

Trial identification

Sponsor protocol code	CYD08

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01064141
WHO universal trial number (UTN)	U1111-1111-5855

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon Cedex 07, France, F-69367
Public contact	Senior Director, Clinical Development, Sanofi Pasteur SA, 65 6431 2358, Anh.Wartel-Tram@sanofipasteur.com
Scientific contact	Senior Director, Clinical Development, Sanofi Pasteur SA, 65 6431 2358, Anh.Wartel-Tram@sanofipasteur.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-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	31 July 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 May 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Safety of CYD dengue vaccine after each injection; first injection given alone or co-administered with measles, mumps, rubella (MMR) vaccine (Trimovax).
Dengue vaccinal viremia

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 equipment was 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	18 January 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Philippines: 210
Worldwide total number of subjects	210
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	210
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled from 18 January 2010 to 29 September 2010 at 2 clinical centers in the Philippines.

Pre-assignment

Screening details:

A total of 210 subjects who met all of the inclusion criteria and none of the exclusion criteria were enrolled and randomized.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

For all groups, the first injection of CYD dengue vaccine was performed under a modified double-blind process where only the person who administered the injection knew which product had been administered. To maintain the modified double-blind process for the sequential versus co-administration of MMR with the first injection of CYD dengue vaccine, some of the toddlers received one injection of placebo.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

Subjects received a total of 5 injections (Dengue vaccine): First injection - Measles, mumps, rubella (MMR) vaccine (Month-1); Second injection - Dengue vaccine (M0), Third injection - Dengue vaccine (M0+6 months); Fourth injection - Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0+9 months), and Fifth injection - Dengue vaccine (M0+12 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, 1 injection at M0, M0+6 months, and M0+12 months.

Investigational medicinal product name	MMR Vaccine (TRIMOVAX®)
Investigational medicinal product code	065
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL, subcutaneous use, 1 injection at Month-1.

Investigational medicinal product name	PENTAXIM®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular use, 1 injection at M0+9 months.

Arm title	Group 2

Arm description:

Subjects received a total of 5 injections (control): First injection - MMR (Month-1); Second injection; control Varicella vaccine (M0); Third injection; control Hepatitis A vaccine (M0 + 6 months); Fourth injection; Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0 + 9 months), and Fifth injection - control Hepatitis A vaccine (M0+12 months).

Arm type	Active comparator
Investigational medicinal product name	MMR Vaccine (TRIMOVAX®)
Investigational medicinal product code	065
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL, subcutaneous use, 1 injection at Month-1.

Investigational medicinal product name	PENTAXIM®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular use, 1 injection at M0+9 months.

Investigational medicinal product name	OKAVAX®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL, subcutaneous use, 1 injection at M0.

Investigational medicinal product name	AVAXIM® 80U
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular use, 1 injection at M0+6 months and M0+12 months.

Arm title	Group 3

Arm description:

Subjects received a total of 6 injections: First injection - control Varicella vaccine (Month-1); Second Dengue vaccine and third MMR injections (M0); Fourth injection; Dengue vaccine (M0+6 months); Fifth injection - Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0+9 months), and Sixth injection; Dengue vaccine (M0+12 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, 1 injection at M0, M0+6 months, and M0+12 months.	
Investigational medicinal product name	OKAVAX®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
0.5 mL, subcutaneous use, 1 injection at Month-1.	
Investigational medicinal product name	PENTAXIM®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL, intramuscular use, 1 injection at M0+9 months.	
Investigational medicinal product name	MMR vaccine (TRIMOVAX®)
Investigational medicinal product code	065
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
0.5 mL, subcutaneous use, 1 injection at M0.	
Arm title	Group 4

Arm description:

Subjects received a total of 6 injections (sequential administration): First injection - MMR (Month-1); Second Dengue vaccine and third placebo injections (M0); Fourth injection - Dengue vaccine (M0+6 months); Fifth injection - Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0+9 months), and Sixth injection - Dengue vaccine (M0+12 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, 1 injection at M0, M0+6 months, and M0+12 months.	
Investigational medicinal product name	MMR vaccine (TRIMOVAX®)
Investigational medicinal product code	065
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
0.5 mL, subcutaneous use, 1 injection at Month-1.	
Investigational medicinal product name	PENTAXIM®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL, intramuscular use, 1 injection at M0+9 months.	

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	60	30	60
Completed	58	30	57
Not completed	2	0	3
Serious event	1	-	-
Consent withdrawn by subject	1	-	2
Serious adverse event	-	-	1

Number of subjects in period 1	Group 4
Started	60
Completed	60
Not completed	0
Serious event	-
Consent withdrawn by subject	-
Serious adverse event	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1
Reporting group description:	
Subjects received a total of 5 injections (Dengue vaccine): First injection - Measles, mumps, rubella (MMR) vaccine (Month-1); Second injection - Dengue vaccine (M0), Third injection - Dengue vaccine (M0+6 months); Fourth injection - Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0+9 months), and Fifth injection - Dengue vaccine (M0+12 months).	
Reporting group title	Group 2
Reporting group description:	
Subjects received a total of 5 injections (control): First injection - MMR (Month-1); Second injection; control Varicella vaccine (M0); Third injection; control Hepatitis A vaccine (M0 + 6 months); Fourth injection; Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0 + 9 months), and Fifth injection - control Hepatitis A vaccine (M0+12 months).	
Reporting group title	Group 3
Reporting group description:	
Subjects received a total of 6 injections: First injection - control Varicella vaccine (Month-1); Second Dengue vaccine and third MMR injections (M0); Fourth injection; Dengue vaccine (M0+6 months); Fifth injection - Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0+9 months), and Sixth injection; Dengue vaccine (M0+12 months).	
Reporting group title	Group 4
Reporting group description:	
Subjects received a total of 6 injections (sequential administration): First injection - MMR (Month-1); Second Dengue vaccine and third placebo injections (M0); Fourth injection - Dengue vaccine (M0+6 months); Fifth injection - Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0+9 months), and Sixth injection - Dengue vaccine (M0+12 months)	

Reporting group values	Group 1	Group 2	Group 3
Number of subjects	60	30	60
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)	60	30	60
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	13.4	13.3	12.7
standard deviation	± 1.05	± 0.969	± 0.864
Gender categorical Units: Subjects			
Female	22	12	26
Male	38	18	34

Reporting group values	Group 4	Total	

Number of subjects	60	210	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	60	210	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: months			
arithmetic mean	12.8		
standard deviation	± 0.971	-	
Gender categorical Units: Subjects			
Female	28	88	
Male	32	122	

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description:	
Subjects received a total of 5 injections (Dengue vaccine): First injection - Measles, mumps, rubella (MMR) vaccine (Month-1); Second injection - Dengue vaccine (M0), Third injection - Dengue vaccine (M0+6 months); Fourth injection - Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0+9 months), and Fifth injection - Dengue vaccine (M0+12 months).	
Reporting group title	Group 2
Reporting group description:	
Subjects received a total of 5 injections (control): First injection - MMR (Month-1); Second injection; control Varicella vaccine (M0); Third injection; control Hepatitis A vaccine (M0 + 6 months); Fourth injection; Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0 + 9 months), and Fifth injection - control Hepatitis A vaccine (M0+12 months).	
Reporting group title	Group 3
Reporting group description:	
Subjects received a total of 6 injections: First injection - control Varicella vaccine (Month-1); Second Dengue vaccine and third MMR injections (M0); Fourth injection; Dengue vaccine (M0+6 months); Fifth injection - Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0+9 months), and Sixth injection; Dengue vaccine (M0+12 months).	
Reporting group title	Group 4
Reporting group description:	
Subjects received a total of 6 injections (sequential administration): First injection - MMR (Month-1); Second Dengue vaccine and third placebo injections (M0); Fourth injection - Dengue vaccine (M0+6 months); Fifth injection - Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine (M0+9 months), and Sixth injection - Dengue vaccine (M0+12 months)	

Primary: Percentage of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following Any Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Percentage of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following Any Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[1]
End point description:	
Solicited injection site reactions: Pain, Erythema, Swelling. Grade 3 solicited injection site reactions: Pain, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥5 cm. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability. Grade 3 solicited systemic reactions: Fever, >39.5°C or >103.1°F; Vomiting, ≥6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, >3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, Refused ≥3 feeds/meals or refused most feeds/meals; Irritability, Inconsolable.	
End point type	Primary
End point timeframe:	
Day 0 (pre-vaccination) up to Day 7 post-any vaccination	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	30	59	60
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	20	20	10.2	6.7
Grade 3 Injection site Pain	0	0	0	0
Injection site Erythema	5	16.7	11.9	3.3
Grade 3 Injection site Erythema	0	0	0	0
Injection site Swelling	3.3	10	1.7	1.7
Grade 3 Injection site Swelling	0	0	0	0
Fever	26.7	36.7	42.4	25
Grade 3 Fever	0	0	0	0
Vomiting	13.3	36.7	5.1	5
Grade 3 Vomiting	0	0	0	0
Crying abnormal	23.3	26.7	13.6	11.7
Grade 3 Crying abnormal	0	0	0	0
Drowsiness	8.3	10	3.4	5
Grade 3 Drowsiness	0	0	0	0
Appetite lost	18.3	20	11.9	10
Grade 3 Appetite lost	0	0	0	0
Irritability	31.7	36.7	11.9	20
Grade 3 Irritability	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following First Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Percentage of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following First Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[2]

End point description:

Solicited injection site reactions: Pain, Erythema, Swelling. Grade 3 solicited injection site reactions: Pain, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥5 cm. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability. Grade 3 solicited systemic reactions: Fever, >39.5°C or >103.1°F; Vomiting, ≥6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, >3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, Refused ≥3 feeds/meals or refused most feeds/meals; Irritability, Inconsolable.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) up to Day 7 post-first vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	30	59	60
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	13.3	20	6.8	5
Grade 3 Injection site Pain	0	0	0	0
Injection site Erythema	5	16.7	10.2	3.3
Grade 3 Injection site Erythema	0	0	0	0
Injection site Swelling	3.3	10	1.7	1.7
Grade 3 Injection site Swelling	0	0	0	0
Fever	20	20	28.8	11.7
Grade 3 Fever	0	0	0	0
Vomiting	11.7	30	1.7	1.7
Grade 3 Vomiting	0	0	0	0
Crying abnormal	20	23.3	13.6	10
Grade 3 Crying abnormal	0	0	0	0
Drowsiness	6.7	10	3.4	5
Grade 3 Drowsiness	0	0	0	0
Appetite lost	16.7	16.7	11.9	5
Grade 3 Appetite lost	0	0	0	0
Irritability	26.7	33.3	11.9	18.3
Grade 3 Irritability	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following Second Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Percentage of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following Second Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[3]

End point description:

Solicited injection site reactions: Pain, Erythema, Swelling. Grade 3 solicited injection site reactions: Pain, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥5 cm. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability. Grade 3 solicited systemic reactions: Fever, >39.5°C or >103.1°F; Vomiting, ≥6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, >3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, Refused ≥3 feeds/meals or refused most feeds/meals; Irritability, Inconsolable.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) up to Day 7 post-second vaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	30	58	60
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	5	3.3	1.7	1.7
Grade 3 Injection site Pain	0	0	0	0
Injection site Erythema	0	3.3	1.7	0
Grade 3 Injection site Erythema	0	0	0	0
Injection site Swelling	0	3.3	0	0
Grade 3 Injection site Swelling	0	0	0	0
Fever	3.3	10	8.6	6.7
Grade 3 Fever	0	0	0	0
Vomiting	0	3.3	3.4	1.7
Grade 3 Vomiting	0	0	0	0
Crying abnormal	0	6.7	0	0
Grade 3 Crying abnormal	0	0	0	0
Drowsiness	0	0	0	0
Grade 3 Drowsiness	0	0	0	0
Appetite lost	1.7	6.7	0	3.3
Grade 3 Appetite lost	0	0	0	0
Irritability	3.3	10	0	1.7
Grade 3 Irritability	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following Third Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Percentage of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following Third Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[4]

End point description:

Solicited injection site reactions: Pain, Erythema, Swelling. Grade 3 solicited injection site reactions: Pain, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥5 cm. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability. Grade 3 solicited systemic reactions: Fever, >39.5°C or >103.1°F; Vomiting, ≥6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, >3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, Refused ≥3 feeds/meals or refused most feeds/meals; Irritability, Inconsolable.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) up to Day 7 post-third vaccination

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	30	57	60
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	3.4	0	1.8	0
Grade 3 Injection site Pain	0	0	0	0
Injection site Erythema	0	3.3	0	0
Grade 3 Injection site Erythema	0	0	0	0
Injection site Swelling	0	0	0	0
Grade 3 Injection site Swelling	0	0	0	0
Fever	10.3	6.7	8.8	8.3
Grade 3 Fever	0	0	0	0
Vomiting	1.7	3.3	0	1.7
Grade 3 Vomiting	0	0	0	0
Crying abnormal	3.4	0	0	1.7
Grade 3 Crying abnormal	0	0	0	0
Drowsiness	1.7	0	0	0
Grade 3 Drowsiness	0	0	0	0
Appetite lost	1.7	0	0	3.3
Grade 3 Appetite lost	0	0	0	0
Irritability	3.4	3.3	0	3.3
Grade 3 Irritability	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Non-serotype Specific CYD Viremia after the First Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Percentage of Subjects with Non-serotype Specific CYD Viremia after the First Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[5]

End point description:

Non-specific specific CYD viremia was assessed using yellow fever (YF) real time polymerase chain reaction (RT-PCR).

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) up to Day 8 (post-first vaccination)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	30	57	60
Units: Percentage of subjects				
number (not applicable)				
Viremia detectable	48.3	0	17.5	28.3
Viremia quantified	1.7	0	1.8	1.7

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Seropositivity for Parental Dengue Virus Serotypes Following Each Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Percentage of Subjects with Seropositivity for Parental Dengue Virus Serotypes Following Each Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[6]

End point description:

Neutralizing antibody levels against each of the 4 parental dengue virus serotype strains were measured using the dengue neutralization assay. Seropositivity was defined as subjects with antibody titers ≥10 1/dil against the 4 dengue serotypes.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 28 post-second and third injections for Groups 1 and 2 and post-first, second, and third injections for Groups 3 and 4.

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	30	58	60
Units: Percentage of subjects				
number (not applicable)				
Dengue Parental Serotype 1; Pre-inj. 1 (Screening)	10	3.3	6.9	10
Dengue Parental Serotype 1; Post-inj. 1 (V04)	0	0	19	30
Dengue Parental Serotype 1; Post-inj. 2 (V07)	91.5	23.3	87.9	93.3
Dengue Parental Serotype 1; Post-inj. 1 (V10)	94.8	20	94.7	96.7
Dengue Parental Serotype 2; Pre-inj. 1 (Screening)	18.3	16.7	13.8	10
Dengue Parental Serotype 2; Post-inj. 1 (V04)	0	0	29.3	33.3
Dengue Parental Serotype 2; Post-inj. 2 (V07)	94.9	26.7	94.8	98.3
Dengue Parental Serotype 2; Post-inj. 3 (V10)	96.6	33.3	96.5	100
Dengue Parental Serotype 3; Pre-inj. 1 (Screening)	26.7	23.3	37.9	40.7

Dengue Parental Serotype 3; Post-inj. 1 (V04)	0	0	70.7	86.7
Dengue Parental Serotype 3; Post-inj. 2 (V07)	100	40	100	98.3
Dengue Parental Serotype 3; Post-inj. 3 (V10)	100	36.7	100	100
Dengue Parental Serotype 4; Pre-inj. 1 (Screening)	25	21.4	5.2	16.7
Dengue Parental Serotype 4; Post-inj. 1 (V04)	0	0	53.4	83.3
Dengue Parental Serotype 4; Post-inj. 2 (V07)	100	40	96.6	98.3
Dengue Parental Serotype 4; Post-inj. 3 (V10)	98.3	23.3	96.5	100

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Seropositivity for at Least 1, 2, 3 or 4 Parental Dengue Virus Serotypes Before and After Each Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Percentage of Subjects with Seropositivity for at Least 1, 2, 3 or 4 Parental Dengue Virus Serotypes Before and After Each Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[7]

End point description:

Neutralizing antibody levels of at least 1 , 2, 3 or the 4 parental dengue virus serotype strains were measured using the dengue neutralization assay. Seropositivity was defined as subjects with antibody titers ≥10 1/dil against the 4 dengue serotypes.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 28 post-second and third injections for Groups 1 and 2 and post-first, second, and third injections for Groups 3 and 4.

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	30	58	60
Units: Percentage of subjects				
number (not applicable)				
At least 1 serotype; Pre-inj. 1 (Screening)	38.3	43.3	46.6	46.7
At least 1 serotype; Post-inj. 1 (V04)	0	0	82.8	91.7
At least 1 serotype; Post-inj. 2 (V07)	100	50	100	100
At least 1 serotype; Post-inj. 3 (V10)	100	43.3	100	100
At least 2 serotypes; Pre-inj. 1 (Screening)	21.7	13.3	12.1	15
At least 2 serotypes; Post-inj. 1 (V04)	0	0	53.4	81.7
At least 2 serotypes; Post-inj. 2 (V07)	100	36.7	98.3	100
At least 2 serotypes; Post-inj. 3 (V10)	100	30	100	100

At least 3 serotypes; Pre-inj. 1 (Screening)	11.7	3.3	3.4	8.3
At least 3 serotypes; Post-inj. 1 (V04)	0	0	24.1	38.3
At least 3 serotypes; Post-inj. 2 (V07)	94.9	23.3	93.1	98.3
At least 3 serotypes; Post-inj. 3 (V10)	96.6	26.7	96.5	100
4 serotypes; Pre-inj. 1 (Screening)	8.3	3.3	1.7	6.7
4 serotypes; Post-inj. 1 (V04)	0	0	12.1	21.7
4 serotypes; Post-inj. 2 (V07)	91.5	20	87.9	90
4 serotypes; Post-inj. 3 (V10)	93.1	13.3	91.2	96.7

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Antibodies Against Each Parental Dengue Virus Serotype Before and Following Each Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Geometric Mean Titers (GMTs) of Antibodies Against Each Parental Dengue Virus Serotype Before and Following Each Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[8]

End point description:

Geometric mean titers of antibodies against parental dengue virus serotypes were measured using the dengue neutralization assay.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 28 post-second and third injections for Groups 1 and 2 and post-first, second, and third injections for Groups 3 and 4.

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	30	58	60
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Dengue Parental Serotype 1; Pre-inj. 1 (Screening)	6.39 (5.21 to 7.85)	5.31 (4.69 to 6.02)	5.59 (4.94 to 6.33)	6.18 (5.16 to 7.41)
Dengue Parental Serotype 1; Post-inj. 1 (V04)	0 (0 to 0)	0 (0 to 0)	7.36 (5.9 to 9.18)	10.4 (7.33 to 14.8)
Dengue Parental Serotype 1; Post-inj. 2 (V07)	69.8 (45.4 to 108)	9.04 (5.59 to 14.6)	62.5 (43.8 to 89.1)	73 (51.4 to 104)
Dengue Parental Serotype 1; Post-inj. 3 (V10)	105 (73.8 to 148)	11.5 (5.77 to 22.8)	108 (80.7 to 144)	124 (90.9 to 169)
Dengue Parental Serotype 2; Pre-inj. 1 (Screening)	10 (6.54 to 15.4)	9.73 (5.18 to 18.3)	7.2 (5.3 to 9.77)	7.46 (5.25 to 10.6)
Dengue Parental Serotype 2; Post-inj. 1 (V04)	0 (0 to 0)	0 (0 to 0)	10.6 (7.29 to 15.6)	14.8 (9.26 to 23.7)
Dengue Parental Serotype 2; Post-inj. 2 (V07)	159 (93.1 to 272)	14.5 (6.81 to 30.8)	141 (88.7 to 224)	114 (76.5 to 168)
Dengue Parental Serotype 2; Post-inj. 3 (V10)	147 (99.2 to 219)	15.7 (7.7 to 32)	213 (146 to 311)	176 (121 to 254)

Dengue Parental Serotype 3; Pre-inj. 1 (Screening)	10.1 (6.99 to 14.5)	9.05 (5.8 to 14.1)	13.8 (9.49 to 20)	14.8 (9.5 to 23.1)
Dengue Parental Serotype 3; Post-inj. 1 (V04)	0 (0 to 0)	0 (0 to 0)	30.8 (21 to 45.1)	96 (61.9 to 149)
Dengue Parental Serotype 3; Post-inj. 2 (V07)	249 (170 to 366)	13.9 (8.1 to 23.8)	254 (196 to 329)	288 (197 to 420)
Dengue Parental Serotype 3; Post-inj. 3 (V10)	311 (222 to 436)	13.4 (7.63 to 23.5)	358 (277 to 464)	387 (284 to 527)
Dengue Parental Serotype 4; Pre-inj. 1 (Screening)	8.25 (6.4 to 10.7)	6.98 (5.41 to 9.01)	5.6 (4.9 to 6.4)	6.99 (5.66 to 8.63)
Dengue Parental Serotype 4; Post-inj. 1 (V04)	0 (0 to 0)	0 (0 to 0)	20.5 (13.7 to 30.5)	89.1 (56.8 to 140)
Dengue Parental Serotype 4; Post-inj. 2 (V07)	131 (104 to 166)	10.1 (7.14 to 14.2)	121 (90.7 to 161)	133 (100 to 176)
Dengue Parental Serotype 4; Post-inj. 3 (V10)	143 (107 to 192)	8.16 (5.66 to 11.8)	127 (96 to 169)	160 (131 to 195)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 (post-vaccination) up to Day 28 post-each vaccination.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Group 1

Reporting group description:

Toddlers who received at total of 5 injections (Dengue vaccine): Month-1 (first injection; MMR), M0 (second injection; Dengue vaccine), M0+6 months (third injection; Dengue vaccine), M0+9 months (fourth injection; Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine), and M0+12 months (fifth injection; Dengue vaccine).

Reporting group title	Group 2

Reporting group description:

Toddlers who received at total of 5 injections (control): Month-1 (first injection; MMR), M0 (second injection; control Varicella vaccine), M0+6 months (third injection; control Hepatitis A vaccine), M0+9 months (fourth injection; Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine), and M0+12 months (fifth injection; control Hepatitis A vaccine).

Reporting group title	Group 3

Reporting group description:

Toddlers who received a total of 6 injections: Month-1 (first injection; control Varicella vaccine), M0 (second [Dengue vaccine] and third [MMR] injections), M0+6 months (fourth injection; Dengue vaccine), M0+9 months (fifth injection; Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine), and M0+12 months (sixth injection; Dengue vaccine).

Reporting group title	Group 4

Reporting group description:

Toddlers who received a total of 6 injections (sequential administration): Month-1 (first injection; MMR), M0 (second [Dengue vaccine] and third [placebo] injections), M0+6 months (fourth injection; Dengue vaccine), M0+9 months (fifth injection; Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hib vaccine), and M0+12 months (sixth injection; Dengue vaccine).

Serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	7 / 59 (11.86%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			

subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	3 / 59 (5.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Dengue fever			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 30 (0.00%)	3 / 59 (5.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 30 (3.33%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 4		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 60 (1.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion			

subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Dengue fever			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 60 (40.00%)	15 / 30 (50.00%)	25 / 59 (42.37%)
Nervous system disorders			
Drowsiness (Post-any injection)			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 60 (8.33%)	3 / 30 (10.00%)	2 / 59 (3.39%)
occurrences (all)	5	3	2
General disorders and administration site conditions			

Injection site Pain (Post-any injection)			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 60 (20.00%)	6 / 30 (20.00%)	6 / 59 (10.17%)
occurrences (all)	13	7	10
Injection site Erythema (Post-any injection)			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 60 (5.00%)	5 / 30 (16.67%)	7 / 59 (11.86%)
occurrences (all)	3	7	10
Injection site Swelling (Post-any injection)			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 60 (3.33%)	3 / 30 (10.00%)	1 / 59 (1.69%)
occurrences (all)	2	4	1
Fever (Post-any injection)			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 60 (26.67%)	11 / 30 (36.67%)	25 / 59 (42.37%)
occurrences (all)	20	11	27
Gastrointestinal disorders			
Vomiting (Post-any injection)			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 60 (13.33%)	11 / 30 (36.67%)	3 / 59 (5.08%)
occurrences (all)	8	11	3
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	0 / 59 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Crying abnormal (Post-any injection)			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 60 (23.33%)	8 / 30 (26.67%)	8 / 59 (13.56%)
occurrences (all)	14	9	8
Irritability (Post-any injection)			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 60 (31.67%)	11 / 30 (36.67%)	7 / 59 (11.86%)
occurrences (all)	20	14	7

Infections and infestations			
Gastroenteritis			
subjects affected / exposed	3 / 60 (5.00%)	2 / 30 (6.67%)	3 / 59 (5.08%)
occurrences (all)	3	2	3
Rhinitis			
subjects affected / exposed	0 / 60 (0.00%)	3 / 30 (10.00%)	6 / 59 (10.17%)
occurrences (all)	0	3	6
Subcutaneous abscess			
subjects affected / exposed	0 / 60 (0.00%)	2 / 30 (6.67%)	1 / 59 (1.69%)
occurrences (all)	0	2	1
Upper respiratory tract infection			
subjects affected / exposed	24 / 60 (40.00%)	15 / 30 (50.00%)	19 / 59 (32.20%)
occurrences (all)	30	20	20
Viral infection			
subjects affected / exposed	9 / 60 (15.00%)	1 / 30 (3.33%)	11 / 59 (18.64%)
occurrences (all)	10	1	13
Viral rhinitis			
subjects affected / exposed	3 / 60 (5.00%)	5 / 30 (16.67%)	0 / 59 (0.00%)
occurrences (all)	3	5	0
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 60 (6.67%)	4 / 30 (13.33%)	0 / 59 (0.00%)
occurrences (all)	4	4	0
Metabolism and nutrition disorders			
Appetite lost (Post-any injection)			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 60 (18.33%)	6 / 30 (20.00%)	7 / 59 (11.86%)
occurrences (all)	12	7	7

Non-serious adverse events	Group 4		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 60 (28.33%)		
Nervous system disorders			
Drowsiness (Post-any injection)			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
General disorders and administration site conditions			

Injection site Pain (Post-any injection) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 4 / 60 (6.67%) 7		
Injection site Erythema (Post-any injection) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 2 / 60 (3.33%) 3		
Injection site Swelling (Post-any injection) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 1 / 60 (1.67%) 1		
Fever (Post-any injection) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 15 / 60 (25.00%) 16		
Gastrointestinal disorders Vomiting (Post-any injection) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 3 / 60 (5.00%) 3		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all)	 3 / 60 (5.00%) 4		
Psychiatric disorders Crying abnormal (Post-any injection) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 7 / 60 (11.67%) 7		
Irritability (Post-any injection) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 12 / 60 (20.00%) 14		

Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Subcutaneous abscess			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	17 / 60 (28.33%)		
occurrences (all)	18		
Viral infection			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	6		
Viral rhinitis			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Appetite lost (Post-any injection)			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2010	Administrative edits to revise and update - "Observational" Objectives or Endpoints; definition of a febrile episode; detection of symptomatic dengue cases for homogeneity in the protocol; the time window for the M15 phone call/home visit; and the addition that a "convalescent sample" of 2 mL would be taken in case of suspected symptomatic dengue cases to investigate the relationship between dengue and injection. Other revisions include - statement of applicable exclusion criteria; assessment of febrile convulsions according to the Guideline for definition and collection of cases of febrile convulsions; clarification that toddlers with abnormal biological parameters would be followed up until parameters returned to normal ranges; Specification that wild-type (WT) dengue RT-PCR was tested in acute samples collected from suspected dengue cases, regardless of time of event after injection; and modified the "Interpretation of Results" section.
09 April 2010	Revised study design from a monocenter to multi-center in view of measles outbreak in the Philippines; Acceleration of recruitment rate for Cohort 3 for protection against measles at the earliest possible time; Revision of "Visit Procedures" to notify general practitioners that patients were going to receive MMR injection during the dengue vaccine trial and for Groups 3 and 4. Revision of dengue microneutralization assay to dengue neutralization assay; Pan flavivirus reverse transcriptase polymerase chain reaction (RT-PCR) was changed to dengue screen RT-PCR and the description of the method was adapted in accordance to the changes.
03 February 2011	The lower limit of the normal range for Hemoglobin (Hb) was changed from 10.9 g/dL to 9.9 g/dL and the analysis of secondary objectives on measles, mumps, rubella (MMR) vaccine was revised.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported