Clinical trial results:
Safety of ChimeriVax™ Dengue Tetravalent Vaccine in Subjects Aged 2 to 45 Years in Mexico

Summary

EudraCT number	2014-001706-17
Trial protocol	Outside EU/EEA
Global end of trial date	27 August 2007

Results information

Result version number	v1 (current)
This version publication date	08 February 2016
First version publication date	22 July 2015

Trial information

Trial identification

Sponsor protocol code	CYD06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon cedex 07, France, F-69367
Public contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (0)437 65 60 60, remi.forrat@sanofipasteur.com
Scientific contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (0)437 65 60 60, remi.forrat@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?	Yes
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 February 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 August 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To describe the safety of each injection of ChimeriVax™ Dengue Tetravalent Vaccine in four age groups of subjects: adults (18 to 45), adolescents (12 to 17), children (6 to 11), and children (2 to 5).
- To describe viremia after each injection of ChimeriVax™ Dengue Tetravalent Vaccine in the four age groups of subjects.
- To describe the humoral immune response against dengue before injection, and after each injection of ChimeriVax™ Dengue Tetravalent Vaccine in the four age groups of subjects.

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: -

Actual start date of recruitment	24 January 2006
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	Mexico: 126
Worldwide total number of subjects	126
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)	0
Children (2-11 years)	72

Adolescents (12-17 years)	36
Adults (18-64 years)	18
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled from 02 February 2006 to 23 July 2007 at 2 clinical centers in Mexico.

Pre-assignment

Screening details:

A total of 126 subjects who met all of the inclusion criteria and none of the exclusion criteria were enrolled and vaccinated.

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:

The blind observer method was used for the first vaccination. The delegate study personnel(s)/pharmacist, independent of the safety evaluation and other evaluations, prepared and administered the vaccine. The subjects, Investigator or designated study personnel in charge of safety assessment did not know which treatment or product being administered. Labels on the secondary packaging were also designed to prevent the treatment from being identified.

Arms

Are arms mutually exclusive?	Yes
Arm title	Study Group 1

Arm description:

Subjects who received Sanofi Pasteur's ChimeriVax™ Dengue Tetravalent Vaccine (serotypes 1, 2, 3, and 4) as first, second, and third injections on Day 0, Day 0 + 3.5 months, and Day 0 + 12 months.

Arm type	Experimental
Investigational medicinal product name	ChimeriVax Dengue Tetravalent Vaccine
Investigational medicinal product code	323
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL dose, subcutaneous, administered on Day 0 (1st injection), Day 0 + 3.5 months (2nd injection), and Day 0 + 12 months (3rd injection).

Arm title	Study Group 2

Arm description:

Subjects received Stamaril Pasteur® (Yellow Fever vaccine) as first injection on Day 0 and sanofi pasteur's CYD Dengue vaccine (serotypes 1, 2, 3, and 4) as second injection (Day 0 + 3.5 months) and third injection (Day 0 + 12 months).

Arm type	Experimental
Investigational medicinal product name	ChimeriVax Dengue Tetravalent Vaccine
Investigational medicinal product code	323
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL dose, subcutaneous, administered on Day 0 (1st injection), Day 0 + 3.5 months (2nd injection), and Day 0 + 12 months (3rd injection).

Investigational medicinal product name	Sanofi Pasteur live attenuated YF vaccine (Stamaril Pasteur®)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection into the deltoid region on Day 0 as the first injection

Number of subjects in period 1	Study Group 1	Study Group 2
Started	84	42
Completed	73	35
Not completed	11	7
Consent withdrawn by subject	3	-
Adverse event, non-fatal	4	3
Serious adverse event	1	1
Lost to follow-up	2	-
Protocol deviation	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Study Group 1
Reporting group description:	
Subjects who received Sanofi Pasteur's ChimeriVax™ Dengue Tetravalent Vaccine (serotypes 1, 2, 3, and 4) as first, second, and third injections on Day 0, Day 0 + 3.5 months, and Day 0 + 12 months.	
Reporting group title	Study Group 2
Reporting group description:	
Subjects received Stamaril Pasteur® (Yellow Fever vaccine) as first injection on Day 0 and sanofi pasteur's CYD Dengue vaccine (serotypes 1, 2, 3, and 4) as second injection (Day 0 + 3.5 months) and third injection (Day 0 + 12 months).	

Reporting group values	Study Group 1	Study Group 2	Total
Number of subjects	84	42	126
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)	48	24	72
Adolescents (12-17 years)	24	12	36
Adults (18-64 years)	12	6	18
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	12.1	11.6	
standard deviation	± 9.2	± 7.3	-
Gender categorical			
Units: Subjects			
Female	49	21	70
Male	35	21	56
Study sub-groups by age			
Study subjects were also categorized into 4 sub-groups based on their age as adults, adolescents, and 2 children groups.			
Units: Subjects			
Adults (age 18 to 45 years)	12	6	18
Adolescents (age 12 to 17 years)	24	12	36
Children (age 6 to 11 years)	24	12	36
Children (age 2 to 5 years)	24	12	36

End points

End points reporting groups

Reporting group title	Study Group 1
Reporting group description:	
Subjects who received Sanofi Pasteur's ChimeriVax™ Dengue Tetravalent Vaccine (serotypes 1, 2, 3, and 4) as first, second, and third injections on Day 0, Day 0 + 3.5 months, and Day 0 + 12 months.	
Reporting group title	Study Group 2
Reporting group description:	
Subjects received Stamaril Pasteur® (Yellow Fever vaccine) as first injection on Day 0 and sanofi pasteur's CYD Dengue vaccine (serotypes 1, 2, 3, and 4) as second injection (Day 0 + 3.5 months) and third injection (Day 0 + 12 months).	

Primary: Number of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following the First Vaccination with Sanofi Pasteur's CYD Dengue Vaccine or Yellow Fever Vaccine (Stamaril Pasteur®)

End point title	Number of Subjects Reporting a Solicited Injection-site or Systemic Reactions Following the First Vaccination with Sanofi Pasteur's CYD Dengue Vaccine or Yellow Fever Vaccine (Stamaril Pasteur®)[1]
End point description:	
Solicited injection site: Pain, Erythema, and Edema. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Asthenia. Grade 3 Solicited Injection site reactions: Pain – Incapacitating, unable to perform usual activities; Erythema and Edema - ≥5 cm. Grade 3 Solicited systemic reactions: Fever - ≥39°C axillary; Headache, Malaise, Myalgia, and Asthenia – Prevents daily activity.	
End point type	Primary
End point timeframe:	
Day 0 up to Day 14 post-first 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	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	40		
Units: Number of subjects				
number (not applicable)				
Inj. site Pain; Adults (18-45 y)	1	1		
Inj. site Pain; Adolescents (12-17 y)	5	1		
Inj. site Pain; Children (6-11 y)	10	0		
Inj. site Pain; Children (2-5 y)	6	5		
All Grade 3 Inj. site Pain	0	0		
Inj. site Erythema; Adults (18-45 y)	3	1		
Inj. site Erythema; Adolescents (12-17 y)	0	0		
Inj. site Erythema; Children (6-11 y)	1	1		
Inj. site Erythema; Children (2-5 y)	2	1		
All Grade 3 Inj. site Erythema	0	0		
Inj. site Edema; Adults (18-45 y)	3	1		
Inj. site Edema; Adolescents (12-17 y)	0	0		

Inj. site Edema; Children (6-11 y)	1	0		
Inj. site Edema; Children (2-5 y)	1	1		
All Grade 3 Inj. site Edema	1	0		
Inj. site Fever; Adults (18-45 y)	0	0		
Inj. site Fever; Adolescents (12-17 y)	3	1		
Inj. site Fever; Children (6-11 y)	2	2		
Inj. site Fever; Children (2-5 y)	3	1		
All Grade 3 Inj. site Fever	3	0		
Inj. site Headache; Adults (18-45 y)	6	3		
Inj. site Headache; Adolescents (12-17 y)	13	6		
Inj. site Headache; Children (6-11 y)	9	2		
Inj. site Headache; Children (2-5 y)	4	2		
All Grade 3 Inj. site Headache	1	0		
Inj. site Malaise; Adults (18-45 y)	0	1		
Inj. site Malaise; Adolescents (12-17 y)	3	1		
Inj. site Malaise; Children (6-11 y)	2	1		
Inj. site Malaise; Children (2-5 y)	3	3		
All Grade 3 Inj. site Malaise	0	0		
Inj. site Myalgia; Adults (18-45 y)	5	2		
Inj. site Myalgia; Adolescents (12-17 y)	7	4		
Inj. site Myalgia; Children (6-11 y)	7	2		
Inj. site Myalgia; Children (2-5 y)	5	3		
All Grade 3 Inj. site Myalgia	0	0		
Inj. site Asthenia; Adults (18-45 y)	3	3		
Inj. site Asthenia; Adolescents (12-17 y)	8	2		
Inj. site Asthenia; Children (6-11 y)	2	1		
Inj. site Asthenia; Children (2-5 y)	4	2		
All Grade 3 Inj. site Asthenia	2	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Solicited injection site: Pain, Erythema, and Edema. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Asthenia. Grade 3 Solicited Injection site reactions: Pain – Incapacitating, unable to perform usual activities; Erythema and Edema - ≥5 cm. Grade 3 Solicited systemic reactions: Fever - ≥39°C axillary; Headache, Malaise, Myalgia, and Asthenia – Prevents daily activity.

End point type	Primary

End point timeframe:

Day 0 to Day 14 post-second 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	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	35		
Units: Number of subjects				
number (not applicable)				
Inj. site Pain; Adults (18-45 y)	2	3		
Inj. site Pain; Adolescents (12-17 y)	9	3		
Inj. site Pain; Children (6-11 y)	6	0		
Inj. site Pain; Children (2-5 y)	3	2		
All Grade 3 Inj. site Pain	0	1		
Inj. site Erythema; Adults (18-45 y)	2	0		
Inj. site Erythema; Adolescents (12-17 y)	4	0		
Inj. site Erythema; Children (6-11 y)	3	1		
Inj. site Erythema; Children (2-5 y)	1	1		
All Grade 3 Inj. site Erythema	1	0		
Inj. site Edema; Adults (18-45 y)	0	0		
Inj. site Edema; Adolescents (12-17 y)	1	1		
Inj. site Edema; Children (6-11 y)	4	1		
Inj. site Edema; Children (2-5 y)	0	1		
All Grade 3 Inj. site Edema	0	0		
Inj. site Fever; Adults (18-45 y)	2	1		
Inj. site Fever; Adolescents (12-17 y)	1	0		
Inj. site Fever; Children (6-11 y)	2	1		
Inj. site Fever; Children (2-5 y)	6	0		
All Grade 3 Inj. site Fever	1	0		
Inj. site Headache; Adults (18-45 y)	4	3		
Inj. site Headache; Adolescents (12-17 y)	7	3		
Inj. site Headache; Children (6-11 y)	7	1		
Inj. site Headache; Children (2-5 y)	5	0		
All Grade 3 Inj. site Headache	1	1		
Inj. site Malaise; Adults (18-45 y)	3	3		
Inj. site Malaise; Adolescents (12-17 y)	2	2		
Inj. site Malaise; Children (6-11 y)	3	0		
Inj. site Malaise; Children (2-5 y)	4	2		
All Grade 3 Inj. site Malaise	0	1		
Inj. site Myalgia; Adults (18-45 y)	2	3		
Inj. site Myalgia; Adolescents (12-17 y)	4	3		
Inj. site Myalgia; Children (6-11 y)	5	0		
Inj. site Myalgia; Children (2-5 y)	2	1		
All Grade 3 Inj. site Myalgia	0	1		
Inj. site Asthenia; Adults (18-45 y)	2	2		
Inj. site Asthenia; Adolescents (12-17 y)	6	1		
Inj. site Asthenia; Children (6-11 y)	2	0		
Inj. site Asthenia; Children (2-5 y)	4	0		

All Grade 3 Inj. site Asthenia	0	1		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Solicited injection site: Pain, Erythema, and Edema. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Asthenia. Grade 3 Solicited Injection site reactions: Pain – Incapacitating, unable to perform usual activities; Erythema and Edema - ≥5 cm. Grade 3 Solicited systemic reactions: Fever - ≥39°C axillary; Headache, Malaise, Myalgia, and Asthenia – Prevents daily activity.

End point type	Primary

End point timeframe:

Day 0 to Day 14 post-third 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	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	35		
Units: Number of subjects				
number (not applicable)				
Inj. site Pain	26	8		
Grade 3 Inj. site Pain	0	1		
Inj. site Erythema	7	2		
Grade 3 Inj. site Erythema	0	0		
Inj. site Edema	5	3		
Grade 3 Inj. site Edema	0	0		
Fever	4	2		
Grade 3 Fever	0	0		
Headache	15	7		
Grade 3 Headache	1	2		
Malaise	10	7		
Grade 3 Malaise	1	2		
Myalgia	14	7		
Grade 3 Myalgia	1	1		
Asthenia	11	3		
Grade 3 Asthenia	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Non-serotype Specific CYD Viremia by Flavivirus Reverse Transcriptase Polymerase Chain Reaction After the First Vaccination with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)

End point title	Percentage of Subjects with Non-serotype Specific CYD Viremia by Flavivirus Reverse Transcriptase Polymerase Chain Reaction After the First Vaccination with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)[4]

End point description:

CYD Dengue vaccine and Yellow Fever vaccine virus were assessed using the flavivirus reverse transcriptase-polymerase chain reaction (RT-PCR).

End point type	Primary

End point timeframe:

Day 0 (V01; pre-vaccination) and Day 7 (V01+7) and Day 14 (V01+14) post-first 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	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	42		
Units: Percentage of subjects				
number (not applicable)				
All subjects; Detected viremia (V01)	0	0		
All subjects; Detected viremia (V01+7)	4.9	2.4		
All subjects; Detected viremia (V01+14)	2.4	0		
Adults (18-45 y); Detected viremia (V01)	0	0		
Adults (18-45 y); Detected viremia (V01+7)	8.3	0		
Adults (18-45 y); Detected viremia (V01+14)	8.3	0		
Adolescents (12-17 y); Detected viremia (V01)	0	0		
Adolescents (12-17 y); Detected viremia (V01+7)	4.2	8.3		
Adolescents (12-17 y); Detected viremia (V01+14)	4.2	0		
Children (6-11 y); Detected viremia (V01)	0	0		
Children (6-11 y); Detected viremia (V01+7)	8.7	0		
Children (6-11 y); Detected viremia (V01+14)	0	0		

Children (2-5 y); Detected viremia (V01)	0	0		
Children (2-5 y); Detected viremia (V01+7)	0	0		
Children (2-5 y); Detected viremia (V01+14)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Non-serotype Specific CYD Viremia by Flavivirus Reverse Transcriptase-Polymerase Chain Reaction After the Second Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Percentage of Subjects with Non-serotype Specific CYD Viremia by Flavivirus Reverse Transcriptase-Polymerase Chain Reaction After the Second Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[5]

End point description:

CYD Dengue Vaccine and Yellow Fever vaccine antibodies were assessed using the flavivirus reverse transcriptase-polymerase chain reaction (RT-PCR).

End point type	Primary

End point timeframe:

Day 0 (V06; pre-second vaccination) and Day 7 (V06+7) and Day 14 (V06+14) post-second 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	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	39		
Units: Percentage of subjects				
number (not applicable)				
All subjects; Detected viremia (V06)	0	0		
All subjects; Detected viremia (V06+7)	2.5	10.5		
All subjects; Detected viremia (V06+14)	0	2.6		
Adults (18-45 y); Detected viremia (V06)	0	0		
Adults (18-45 y); Detected viremia (V06+7)	8.3	0		
Adults (18-45 y); Detected viremia (V06+14)	0	0		
Adolescents (12-17 y); Detected viremia (V06)	0	0		
Adolescents (12-17 y); Detected viremia (V06+7)	0	8.3		
Adolescents (12-17 y); Detected viremia (V06+14)	0	8.3		
Children (6-11 y); Detected viremia (V06)	0	0		
Children (6-11 y); Detected viremia (V06+7)	0	20		

Children (6-11 y); Detected viremia (V06+14)	0	0		
Children (2-5 y); Detected viremia (V06)	0	0		
Children (2-5 y); Detected viremia (V06+7)	5	10		
Children (2-5 y); Detected viremia (V06+14)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Non-serotype Specific CYD Viremia by Yellow Fever Flavivirus Reverse Transcriptase-Polymerase Chain Reaction After the Second Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Percentage of Subjects with Non-serotype Specific CYD Viremia by Yellow Fever Flavivirus Reverse Transcriptase-Polymerase Chain Reaction After the Second Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[6]

End point description:

Antibodies to CYD Dengue vaccine and Yellow Fever vaccine antigens were assessed using the Yellow Fever Flavivirus reverse transcriptase-polymerase chain reaction (RT-PCR).

End point type	Primary

End point timeframe:

Day 0 (V06; pre-second vaccination) and Day 7 (V06+7) and Day 14 (V06+14) post-second vaccination

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	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	39		
Units: Percentage of subjects				
number (not applicable)				
All subjects; Detected viremia (V06)	0	0		
All subjects; Detected viremia (V06+7)	2.5	26.3		
All subjects; Detected viremia (V06+14)	2.6	12.8		
Adults (18-45 y); Detected viremia (V06)	0	0		
Adults (18-45 y); Detected viremia (V06+7)	0	50		
Adults (18-45 y); Detected viremia (V06+14)	0	0		
Adolescents (12-17 y); Detected viremia (V06)	0	0		
Adolescents (12-17 y); Detected viremia (V06+7)	8.3	33.3		
Adolescents (12-17 y); Detected viremia (V06+14)	4.2	16.7		
Children (6-11 y); Detected viremia (V06)	0	0		

Children (6-11 y); Detected viremia (V06+7)	0	20		
Children (6-11 y); Detected viremia (V06+14)	4.3	20		
Children (2-5 y); Detected viremia (V06)	0	0		
Children (2-5 y); Detected viremia (V06+7)	0	10		
Children (2-5 y); Detected viremia (V06+14)	0	9.1		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Non-serotype Specific CYD Viremia by Flavivirus Reverse Transcriptase-Polymerase Chain Reaction After the Third Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Percentage of Subjects with Non-serotype Specific CYD Viremia by Flavivirus Reverse Transcriptase-Polymerase Chain Reaction After the Third Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[7]

End point description:

Antibodies to CYD Dengue vaccine and Yellow Fever vaccine antigens were assessed using the Yellow Fever Flavivirus reverse transcriptase-polymerase chain reaction (RT-PCR).

End point type	Primary

End point timeframe:

Day 0 (V11; pre-third vaccination) and Day 7 (V11+7) post-third vaccination

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	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	35		
Units: Percentage of subjects				
number (not applicable)				
All subjects; Detected viremia (V11)	1.4	0		
All subjects; Detected viremia (V11+7)	2.8	8.8		
Adults (18-45 y); Detected viremia (V11)	0	0		
Adults (18-45 y); Detected viremia (V11+7)	8.3	0		
Adolescents (12-17 y); Detected viremia (V11)	4.2	0		
Adolescents (12-17 y); Detected viremia (V11+7)	0	0		
Children (6-11 y); Detected viremia (V11)	0	0		
Children (6-11 y); Detected viremia (V11+7)	5	30		
Children (2-5 y); Detected viremia (V11)	0	0		

Children (2-5 y); Detected viremia (V11+7)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Non-serotype Specific CYD Viremia by Yellow Fever Reverse Transcriptase-Polymerase Chain Reaction After the Third Vaccination with Sanofi Pasteur's CYD Dengue Vaccine

End point title	Percentage of Subjects with Non-serotype Specific CYD Viremia by Yellow Fever Reverse Transcriptase-Polymerase Chain Reaction After the Third Vaccination with Sanofi Pasteur's CYD Dengue Vaccine[8]

End point description:

Antibodies to CYD Dengue vaccine and Yellow Fever vaccine antigens were assessed using the Yellow Fever Flavivirus reverse transcriptase-polymerase chain reaction (RT-PCR).

End point type	Primary

End point timeframe:

Day 0 (V11; pre-third vaccination) and Day 7 (V11+7) post-third vaccination

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	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	35		
Units: Percentage of subjects				
number (not applicable)				
All subjects; Detected viremia (V11)	1.4	0		
All subjects; Detected viremia (V11+7)	5.6	26.5		
Adults (18-45 y); Detected viremia (V11)	0	0		
Adults (18-45 y); Detected viremia (V11+7)	0	33.3		
Adolescents (12-17 y); Detected viremia (V11)	0	0		
Adolescents (12-17 y); Detected viremia (V11+7)	4.2	12.5		
Children (6-11 y); Detected viremia (V11)	5	0		
Children (6-11 y); Detected viremia (V11+7)	10	20		
Children (2-5 y); Detected viremia (V11)	0	0		
Children (2-5 y); Detected viremia (V11+7)	6.3	40		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers of Neutralizing Antibodies Against Dengue Serotype Strain 1 Before and Following Each Injection with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)

End point title	Geometric Mean Titers of Neutralizing Antibodies Against Dengue Serotype Strain 1 Before and Following Each Injection with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)

End point description:

Neutralizing antibody levels against each of the four parental dengue virus serotype strains of ChimeriVax™ Dengue Tetravalent Vaccine constructs, and against the Thai Mahidol four dengue virus serotype strains were assessed by the Plaque Reduction Neutralization Test, (PRNT)

End point type	Primary

End point timeframe:

Day 0 (pre-first, second, and third vaccination) and Day 28 post-first, second, and third post-vaccination

End point values	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	42		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Parental Dengue 1 Strain; Pre-first vaccination	5 (5 to 5)	5 (5 to 5)		
Parental Dengue 1 Strain; Post-first vaccination	6.17 (5.46 to 6.97)	5.81 (4.99 to 6.77)		
Parental Dengue 1 Strain; Pre-second vaccination	5.48 (4.98 to 6.04)	5.71 (4.99 to 6.54)		
Parental Dengue 1 Strain; Post-second vaccination	14.2 (10.6 to 19)	15.2 (10.4 to 22)		
Parental Dengue 1 Strain; Pre-third vaccination	6.6 (5.63 to 7.74)	6.34 (5.21 to 7.71)		
Parental Dengue 1 Strain; Post-third vaccination	35.6 (26.4 to 47.9)	43.4 (29 to 64.9)		
Mahidol Dengue 1 Strain; Pre-first vaccination	5 (5 to 5)	5 (5 to 5)		
Mahidol Dengue 1 Strain; Post-first vaccination	7.45 (6.1 to 9.1)	5.65 (4.88 to 6.53)		
Mahidol Dengue 1 Strain; Pre-second vaccination	7.04 (5.85 to 8.46)	5.46 (4.82 to 6.2)		
Mahidol Dengue 1 Strain; Post-second vaccination	17.5 (12.6 to 24.4)	11.5 (7.81 to 16.9)		
Mahidol Dengue 1 Strain; Pre-third vaccination	7.07 (5.86 to 8.54)	8.14 (5.99 to 11.1)		
Mahidol Dengue 1 Strain; Post-third vaccination	35.7 (24.8 to 51.6)	31.7 (21 to 48)		

Statistical analyses

Statistical analysis title	P-value test comparing GMT pre- and post-injection

Statistical analysis description:

P-values for tests comparing GMTs after vaccinations between vaccine groups are adjusted on age groups. ANCOVA models performed on Log10 distributions after vaccinations adjusted on age groups and on Log10 distributions before vaccinations.

Comparison groups	Study Group 1 v Study Group 2
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[9]
P-value	= 0.5656 [10]
Method	ANCOVA

Notes:

[9] - Intra-group comparisons were assessed in pre-first, second, and third injection (inj.) vs. post-first, second, and third inj.

[10] - Grp 1; Parental: Pre-each inj. vs. Post-each inj. was P=0.5656, 0.9408; and 0.5194, respectively. Mahidol: P=0.0723, 0.3274, and 0.2250. Grp 2; Parental: P=0.5656, 0.9408, 0.5194. Mahidol: P=0.0723, 0.3274, and 0.2250.

Primary: Geometric Mean Titers of Neutralizing Antibodies Against Dengue Serotype Strain 2 Before and Following Each Injection with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)

End point title	Geometric Mean Titers of Neutralizing Antibodies Against Dengue Serotype Strain 2 Before and Following Each Injection with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)

End point description:

Neutralizing antibody levels against each of the four parental dengue virus serotype strains of ChimeriVax™ Dengue Tetravalent Vaccine constructs, and against the Thai Mahidol four dengue virus serotype strains were assessed by the Plaque Reduction Neutralization Test, (PRNT).

End point type	Primary

End point timeframe:

Day 0 (pre-first, second, and third vaccination) and Day 28 post-first, second, and third post-vaccination

End point values	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	42		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Parental Dengue 2 Strain; Pre-first vaccination	5 (5 to 5)	5.32 (4.69 to 6.04)		
Parental Dengue 2 Strain; Post-first vaccination	11.2 (8.52 to 14.8)	6.18 (4.84 to 7.9)		
Parental Dengue 2 Strain; Pre-second vaccination	10.2 (8.11 to 12.7)	5.62 (4.65 to 6.81)		
Parental Dengue 2 Strain; Post-second vaccination	32.3 (23.9 to 43.7)	23.5 (15.6 to 35.6)		
Parental Dengue 2 Strain; Pre-third vaccination	10.9 (8.54 to 14)	10.5 (7.24 to 15.2)		
Parental Dengue 2 Strain; Post-third vaccination	53.6 (40.4 to 71.1)	58 (37.6 to 89.6)		
Mahidol Dengue 2 Strain; Pre-first vaccination	5 (5 to 5)	5.29 (4.72 to 5.92)		
Mahidol Dengue 2 Strain; Post-first vaccination	11.7 (8.57 to 16.1)	6.69 (4.99 to 8.96)		

Mahidol Dengue 2 Strain; Pre-second vaccination	6.48 (5.57 to 7.55)	5.47 (4.56 to 6.56)		
Mahidol Dengue 2 Strain; Post-second vaccination	9.32 (7.4 to 11.7)	6.48 (4.76 to 8.83)		
Mahidol Dengue 2 Strain; Pre-third vaccination	5.48 (5 to 6.01)	6.18 (4.85 to 7.88)		
Mahidol Dengue 2 Strain; Post-third vaccination	11.9 (9 to 15.7)	9.6 (6.54 to 14.1)		

Statistical analyses

Statistical analysis title	P-value test comparing GMT pre- and post-injection

Statistical analysis description:

P-values for tests comparing GMTs after vaccinations between vaccine groups are adjusted on age groups. ANCOVA models performed on Log10 distributions after vaccinations adjusted on age groups and on Log10 distributions before vaccinations.

Comparison groups	Study Group 1 v Study Group 2
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	= 0.0003 [12]
Method	ANCOVA

Notes:

[11] - Intra-group comparisons were assessed in pre-first, second, and third injection (inj.) vs. post-first, second, and third inj.
[12] - Grp 1; Parental: Pre-each inj. vs. Post-each inj. was P=0.0003, 0.6049; and 0.8375, respectively. Mahidol: P=0.0033, 0.1651, and 0.0759. Grp 2; Parental: P=0.0003, 0.6049, 0.8375. Mahidol: P=0.0033, 0.1651, and 0.0759.

Primary: Geometric Mean Titers of Neutralizing Antibodies Against Dengue Serotype Strain 3 Before and Following Each Injection with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)

End point title	Geometric Mean Titers of Neutralizing Antibodies Against Dengue Serotype Strain 3 Before and Following Each Injection with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)

End point description:

Neutralizing antibody levels against each of the four parental dengue virus serotype strains of ChimeriVax™Dengue Tetravalent Vaccine constructs and against the Thai Mahidol four dengue virus serotype strains were assessed using the Plaque Reduction Neutralization Test (PRNT).

End point type	Primary

End point timeframe:

Day 0 (pre-first, second, and third vaccination) and Day 28 post-first, second, and third post-vaccination

End point values	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	42		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Parental Dengue 3 Strain; Pre-first vaccination	5.11 (4.96 to 5.26)	5 (5 to 5)		

Parental Dengue 3 Strain; Post-first vaccination	15.5 (11.5 to 20.9)	5.7 (4.84 to 6.71)		
Parental Dengue 3 Strain; Pre-second vaccination	11.2 (8.88 to 14.2)	6.01 (4.98 to 7.26)		
Parental Dengue 3 Strain; Post-second vaccination	26.8 (20.3 to 35.4)	25.8 (17.4 to 38.3)		
Parental Dengue 3 Strain; Pre-third vaccination	9.76 (7.84 to 12.1)	6.93 (5.58 to 8.59)		
Parental Dengue 3 Strain; Post-third vaccination	51.7 (41.5 to 64.4)	48.3 (34.2 to 68.3)		
Mahidol Dengue 3 Strain; Pre-first vaccination	5 (5 to 5)	5.22 (4.78 to 5.71)		
Mahidol Dengue 3 Strain; Post-first vaccination	11.6 (8.48 to 15.7)	5.59 (4.91 to 6.36)		
Mahidol Dengue 3 Strain; Pre-second vaccination	7.98 (6.53 to 9.74)	5.1 (4.9 to 5.32)		
Mahidol Dengue 3 Strain; Post-second vaccination	17 (13 to 22.2)	10.6 (7.45 to 15.2)		
Mahidol Dengue 3 Strain; Pre-third vaccination	6.56 (5.62 to 7.66)	5.57 (5.01 to 6.2)		
Mahidol Dengue 3 Strain; Post-third vaccination	24.2 (18.8 to 31.3)	24.3 (16.1 to 36.7)		

Statistical analyses

Statistical analysis title	P-value test comparing GMT pre- and post-injection

Statistical analysis description:

P-values for tests comparing GMTs after vaccinations between vaccine groups are adjusted on age groups. ANCOVA models performed on Log10 distributions after vaccinations adjusted on age groups and on Log10 distributions before vaccinations.

Comparison groups	Study Group 1 v Study Group 2
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	< 0.0001 [14]
Method	ANCOVA

Notes:

[13] - Intra-group comparisons were assessed pre-first, second, and third injection (inj.) vs. post-first, second, and third inj.
[14] - Grp 1; Parental: Pre-each inj. vs. Post-each inj. was P<0.0001, 0.2976; and 0.8712, respectively. Mahidol: P=0.0011, 0.5503, and 0.9928. Grp 2; Parental: P<0.0001, 0.2976, 0.8712. Mahidol: P=0.0011, 0.5503, and 0.9928.

Primary: Geometric Mean Titers of Neutralizing Antibodies Against Yellow Fever Before and Following Vaccination with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)

End point title	Geometric Mean Titers of Neutralizing Antibodies Against Yellow Fever Before and Following Vaccination with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)[15]

End point description:

Neutralizing antibody levels against Yellow Fever antigens were assessed using the Plaque Reduction Neutralization Test (PRNT).

End point type	Primary

End point timeframe:

Day 0 (pre-first [V01] and second vaccination [V06]) and Day 28 post-first (V04) and second (V09)

post-vaccination

Notes:

[15] - 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	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	40		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
All; Pre-first inj. (V01)	2.5 (2.5 to 2.5)	2.5 (2.5 to 2.5)		
All; Post-first inj. (V04)	2.88 (2.49 to 3.32)	80.9 (53.6 to 122)		
All; Pre-second inj. (V06)	2.66 (2.42 to 2.93)	111 (69.5 to 178)		
All; Post-second inj. (V09)	2.67 (2.41 to 2.95)	176 (111 to 280)		
Adults (18-45 y); Pre-first inj. (V01)	2.5 (2.5 to 2.5)	2.5 (2.5 to 2.5)		
Adults (18-45 y); Post-first inj. (V04)	2.5 (2.5 to 2.5)	148 (69.8 to 313)		
Adults (18-45 y); Pre-second inj. (V06)	2.5 (2.5 to 2.5)	108 (54.7 to 212)		
Adults (18-45 y); Post-second inj. (V09)	2.5 (2.5 to 2.5)	147 (93.7 to 230)		
Adolescents (12-17 y); Pre-first inj. (V01)	2.5 (2.5 to 2.5)	2.5 (2.5 to 2.5)		
Adolescents (12-17 y); Post-first inj. (V04)	2.69 (2.31 to 3.14)	203 (114 to 359)		
Adolescents (12-17 y); Pre-second inj. (V06)	2.5 (2.5 to 2.5)	301 (169 to 536)		
Adolescents (12-17 y); Post-second inj. (V09)	2.5 (2.5 to 2.5)	321 (167 to 618)		
Children (6-11 y); Pre-first inj. (V01)	2.5 (2.5 to 2.5)	2.5 (2.5 to 2.5)		
Children (6-11 y); Post-first inj. (V04)	2.5 (2.5 to 2.5)	38.5 (17.2 to 86.2)		
Children (6-11 y); Pre-second inj. (V06)	2.5 (2.5 to 2.5)	95.7 (31.8 to 288)		
Children (6-11 y); Post-second inj. (V09)	2.5 (2.5 to 2.5)	167 (44.1 to 633)		
Children (2-5 y); Pre-first inj. (V01)	2.5 (2.5 to 2.5)	2.5 (2.5 to 2.5)		
Children (2-5 y); Post-first inj. (V04)	3.95 (2.32 to 6.71)	45.6 (19.1 to 109)		
Children (2-5 y); Pre-second inj. (V06)	3.19 (2.16 to 4.72)	43.7 (15 to 127)		
Children (2-5 y); Post-second inj. (V09)	3.26 (2.12 to 5)	93.7 (26.9 to 327)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects with Antibody titer ≥ 10 (1/dil) Against Yellow

Fever Antigen Before and Following Vaccination with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)

End point title	Percentage of Subjects with Antibody titer ≥ 10 (1/dil) Against Yellow Fever Antigen Before and Following Vaccination with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever Vaccine (Stamaril Pasteur®)[16]

End point description:

Neutralizing antibody levels against Yellow Fever antigens were assessed using the Plaque Reduction Neutralization Test (PRNT).

End point type	Primary

End point timeframe:

Day 0 (pre-first [V01] and second vaccination [V06]) and Day 28 post-first (V04) and second (V09) post-vaccination

Notes:

[16] - 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	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	40		
Units: Percentage of subjects				
number (not applicable)				
All; Pre-first inj. (V01)	0	0		
All; Post-first inj. (V04)	4.9	95		
All; Pre-second inj. (V06)	1.3	92.3		
All; Post-second inj. (V09)	1.3	94.4		
Adults (18-45 y); Pre-first inj. (V01)	0	0		
Adults (18-45 y); Post-first inj. (V04)	0	100		
Adults (18-45 y); Pre-second inj. (V06)	0	100		
Adults (18-45 y); Post-second inj. (V09)	0	100		
Adolescents (12-17 y); Pre-first inj. (V01)	0	0		
Adolescents (12-17 y); Post-first inj. (V04)	4.2	100		
Adolescents (12-17 y); Pre-second inj. (V06)	0	100		
Adolescents (12-17 y); Post-second inj. (V09)	0	100		
Children (6-11 y); Pre-first inj. (V01)	0	0		
Children (6-11 y); Post-first inj. (V04)	0	91.7		
Children (6-11 y); Pre-second inj. (V06)	0	90		
Children (6-11 y); Post-second inj. (V09)	0	88.9		
Children (2-5 y); Pre-first inj. (V01)	0	0		
Children (2-5 y); Post-first inj. (V04)	14.3	90		
Children (2-5 y); Pre-second inj. (V06)	5	81.8		
Children (2-5 y); Post-second inj. (V09)	5.3	88.9		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies Against Dengue Serotype Strain 4 Before and Following Each Injection with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever (YF) vaccine (Stamaril Pasteur®)

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies Against Dengue Serotype Strain 4 Before and Following Each Injection with Sanofi Pasteur's CYD Dengue Vaccine and Yellow Fever (YF) vaccine (Stamaril Pasteur®)

End point description:

Neutralizing antibody levels against each of the four parental dengue virus serotype strains of ChimeriVax™ Dengue Tetravalent Vaccine constructs and against the Thai Mahidol four dengue virus serotype strains were assessed using the Plaque Reduction Neutralization Test (PRNT).

End point type	Primary

End point timeframe:

Day 0 (pre-first, second, and third vaccination) and Day 28 post-first, second, and third post-vaccination

End point values	Study Group 1	Study Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	42		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Parental Dengue 4 Strain; Pre-first vaccination	5 (5 to 5)	5 (5 to 5)		
Parental Dengue 4 Strain; Post-first vaccination	80.4 (49.2 to 131)	6.74 (4.69 to 9.69)		
Parental Dengue 4 Strain; Pre-second vaccination	21.9 (16 to 29.9)	5.9 (4.88 to 7.14)		
Parental Dengue 4 Strain; Post-second vaccination	47.2 (36 to 61.8)	54.8 (28.5 to 105)		
Parental Dengue 4 Strain; Pre-third vaccination	17.8 (13.3 to 23.9)	16.7 (10.8 to 26)		
Parental Dengue 4 Strain; Post-third vaccination	71.7 (54.7 to 93.9)	85.1 (57.7 to 126)		
Mahidol Dengue 4 Strain; Pre-first vaccination	5.48 (5.08 to 5.91)	5.13 (4.87 to 5.41)		
Mahidol Dengue 4 Strain; Post-first vaccination	155 (94 to 256)	8.46 (5.45 to 13.1)		
Mahidol Dengue 4 Strain; Pre-second vaccination	33.1 (23.6 to 46.5)	5.83 (4.94 to 6.89)		
Mahidol Dengue 4 Strain; Post-second vaccination	62.4 (46.6 to 83.5)	58.7 (28.2 to 122)		
Mahidol Dengue 4 Strain; Pre-third vaccination	20.7 (15.4 to 27.8)	16.1 (10 to 25.7)		
Mahidol Dengue 4 Strain; Post-third vaccination	82.4 (63.5 to 107)	74.7 (50.8 to 110)		

Statistical analyses

Statistical analysis title	P-value test comparing GMT pre- and post-injection

Statistical analysis description:

P-values for tests comparing GMTS after vaccinations between vaccine groups are adjusted on age groups. ANCOVA models performed on Log10 distributions after vaccinations adjusted on age groups and on Log10 distributions before vaccinations.

Comparison groups	Study Group 1 v Study Group 2
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	< 0.0001 [18]
Method	ANCOVA

Notes:

[17] - Intra-group comparisons were assessed in pre-first, second, and third injection (inj.) vs. post-first, second, and third inj.

[18] - Grp 1; Parental: Pre-each inj. vs. Post-each inj. was P<0.0001, 0.0183, and 0.4596, respectively. Mahidol: P<0.0001, 0.0094, and 0.7019. Grp 2; Parental: P<0.0001, 0.0183, 0.4596. Mahidol: P<0.0001, 0.0094, and 0.7019.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events data were collected from Day 0 up to 28 days after each vaccination.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	7.1

Reporting groups	
Reporting group title	CYD TV/CYD TV
Reporting group description:	
Subjects who received Sanofi Pasteur's ChimeriVax™ dengue Tetravalent Vaccine (CYD TV; serotypes 1, 2, 3, and 4) as first, second, and third injections on Day 0, Day 0 + 3.5 months, and Day 0 + 12 months.	
Reporting group title	YFV/CYD
Reporting group description:	
Stamaril Pasteur® as first injection on Day 0 and sanofi pasteur's CYD TV (serotypes 1, 2, 3, and 4) as second and third injections on Day 0 + 3.5 months and Day 0 + 12 months, respectively.	

Serious adverse events	CYD TV/CYD TV	YFV/CYD	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 84 (2.38%)	2 / 42 (4.76%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 84 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Partial seizures			
subjects affected / exposed	1 / 84 (1.19%)	0 / 42 (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			
Hepatitis A			
subjects affected / exposed	1 / 84 (1.19%)	0 / 42 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Upper respiratory tract infection			
subjects affected / exposed	0 / 84 (0.00%)	1 / 42 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CYD TV/CYD TV	YFV/CYD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 84 (38.10%)	11 / 42 (26.19%)	
Nervous system disorders			
Headache; Post-first vaccination			
alternative assessment type: Systematic			
subjects affected / exposed	32 / 84 (38.10%)	8 / 42 (19.05%)	
occurrences (all)	32	8	
General disorders and administration site conditions			
Inj. site Pain; Post-third vaccination			
alternative assessment type: Systematic			
subjects affected / exposed[1]	26 / 73 (35.62%)	8 / 35 (22.86%)	
occurrences (all)	26	8	
Inj. site Erythema; Post-second vaccination			
alternative assessment type: Systematic			
subjects affected / exposed[2]	10 / 77 (12.99%)	3 / 39 (7.69%)	
occurrences (all)	10	3	
Inj. site Edema; Post-third vaccination			
alternative assessment type: Systematic			
subjects affected / exposed[3]	5 / 73 (6.85%)	3 / 35 (8.57%)	
occurrences (all)	5	3	
Fever; Post-second vaccination			
alternative assessment type: Systematic			
subjects affected / exposed[4]	11 / 77 (14.29%)	4 / 39 (10.26%)	
occurrences (all)	11	4	
Malaise; Post-first vaccination			
alternative assessment type: Systematic			

subjects affected / exposed	21 / 84 (25.00%)	7 / 42 (16.67%)	
occurrences (all)	21	7	
Asthenia; Post-second vaccination alternative assessment type: Systematic			
subjects affected / exposed[5]	14 / 77 (18.18%)	8 / 39 (20.51%)	
occurrences (all)	14	8	
Musculoskeletal and connective tissue disorders			
Myalgia; Post-first vaccination alternative assessment type: Systematic			
subjects affected / exposed	24 / 84 (28.57%)	11 / 42 (26.19%)	
occurrences (all)	24	11	

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: This was a solicited adverse event recorded in a diary card within 14 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[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: This was a solicited adverse event recorded in a diary card within 14 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[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: This was a solicited adverse event recorded in a diary card within 14 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[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: This was a solicited adverse event recorded in a diary card within 14 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[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: This was a solicited adverse event recorded in a diary card within 14 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported