



## Clinical trial results: Immunogenicity and Safety of a Single Dose of SP093 Typhoid Vi Polysaccharide Vaccine Given in Japanese Subjects

### Summary

EudraCT number	2015-005195-22
Trial protocol	Outside EU/EEA
Global end of trial date	28 September 2012

### Results information

Result version number	v1 (current)
This version publication date	03 March 2016
First version publication date	03 March 2016

### Trial information

#### Trial identification

Sponsor protocol code	TYP31(SFY12079)
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01608815
WHO universal trial number (UTN)	U1111-1124-7699

Notes:

### Sponsors

Sponsor organisation name	Sanofi Pasteur KK
Sponsor organisation address	3-20-2, Nishi Shinjuku, Shinjuku-ku, Tokyo, Japan, 163-1488
Public contact	Medical Director, Sanofi Pasteur KK, 81 3 6301 3603, Toshihiro.emori@sanofi.com
Scientific contact	Medical Director, Sanofi Pasteur KK, 81 3 6301 3603, Toshihiro.emori@sanofi.com

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 December 2012
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	28 September 2012
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

1. To describe the seroconversion rate (percentage of subjects with at least a 4-fold increase of their Vi antibody titer) between Day 0 before vaccination and Day 28 after vaccination with typhoid Vi polysaccharide (SP093) vaccine in subjects aged 2 years and above.

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	26 May 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 200
Worldwide total number of subjects	200
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)	5
Adolescents (12-17 years)	7
Adults (18-64 years)	188

From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study subjects were enrolled from 26 May 2012 to 31 August 2012 at 4 clinic centers in Japan.

### Pre-assignment

Screening details:

A total of 200 subjects who met all of the inclusion and none of the exclusion criteria were vaccinated in this study.

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Adults (Group 1)

Arm description:

Subjects  $\geq 18$  years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.

Arm type	Experimental
Investigational medicinal product name	SP093, Typhoid Vi Polysaccharide Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection on Day 0 (Visit 1).

<b>Arm title</b>	Adolescents (Group 2)
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Arm description:

Subjects 12 to 17 years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.

Arm type	Experimental
Investigational medicinal product name	SP093, Typhoid Vi Polysaccharide Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection on Day 0 (Visit 1).

<b>Arm title</b>	Children (Group 3)
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Arm description:

Subjects 2 to 11 years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.

Arm type	Experimental
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Investigational medicinal product name	SP093, Typhoid Vi Polysaccharide Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection on Day 0 (Visit 1).

<b>Number of subjects in period 1</b>	Adults (Group 1)	Adolescents (Group 2)	Children (Group 3)
Started	188	7	5
Completed	188	7	5

## Baseline characteristics

### Reporting groups

Reporting group title	Adults (Group 1)
Reporting group description:	
Subjects $\geq 18$ years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.	
Reporting group title	Adolescents (Group 2)
Reporting group description:	
Subjects 12 to 17 years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.	
Reporting group title	Children (Group 3)
Reporting group description:	
Subjects 2 to 11 years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.	

Reporting group values	Adults (Group 1)	Adolescents (Group 2)	Children (Group 3)
Number of subjects	188	7	5
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)	0	0	5
Adolescents (12-17 years)	0	7	0
Adults (18-64 years)	188	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	37.2	15.6	5.2
standard deviation	$\pm 11.4$	$\pm 2$	$\pm 3.8$
Gender categorical			
Units: Subjects			
Female	72	3	1
Male	116	4	4

Reporting group values	Total		
Number of subjects	200		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	5		
Adolescents (12-17 years)	7		
Adults (18-64 years)	188		

From 65-84 years	0		
85 years and over	0		

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	76		
Male	124		

## End points

### End points reporting groups

Reporting group title	Adults (Group 1)
Reporting group description:	
Subjects $\geq 18$ years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.	
Reporting group title	Adolescents (Group 2)
Reporting group description:	
Subjects 12 to 17 years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.	
Reporting group title	Children (Group 3)
Reporting group description:	
Subjects 2 to 11 years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.	

### Primary: Number of Subjects With At Least a 4-Fold Rise in Vi Antibody Titers Following Vaccination With a Typhoid Vi Polysaccharide Vaccine

End point title	Number of Subjects With At Least a 4-Fold Rise in Vi Antibody Titers Following Vaccination With a Typhoid Vi Polysaccharide Vaccine <sup>[1]</sup>
End point description:	
Anti-Vi antibodies were measured by enzyme-linked immunosorbent assay (ELISA).	
End point type	Primary
End point timeframe:	
Day 0 (pre-vaccination) to Day 28 (post-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	Adults (Group 1)	Adolescents (Group 2)	Children (Group 3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	7	5	
Units: Number of subjects				
number (not applicable)				
Subjects With a 4-Fold Rise in Vi Antibody Titers	173	6	5	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Titers (GMTs) of Antibodies to Vi Antibody Before and Following Vaccination With a Typhoid Vi Polysaccharide Vaccine

End point title	Geometric Mean Titers (GMTs) of Antibodies to Vi Antibody Before and Following Vaccination With a Typhoid Vi Polysaccharide Vaccine
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End point description:

Anti-Vi antibodies were measured by enzyme-linked immunosorbent assay (ELISA).



End point type	Secondary
End point timeframe:	
Day 0 (pre-vaccination) and Day 28 post-vaccination	

End point values	Adults (Group 1)	Adolescents (Group 2)	Children (Group 3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	7	5	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
GMT (pre-vaccination)	6.6 (5.8 to 7.4)	10.2 (2.9 to 35.9)	3.7 (3.7 to 3.7)	
GMT (post-vaccination)	148.6 (126.9 to 174)	320 (230.6 to 444.2)	501.7 (305.3 to 824.5)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Titer Ratios (GMTRs) of Antibodies to Vi Antibody Following Vaccination With a Typhoid Vi Polysaccharide Vaccine

End point title	Geometric Mean Titer Ratios (GMTRs) of Antibodies to Vi Antibody Following Vaccination With a Typhoid Vi Polysaccharide Vaccine
End point description:	
Anti-Vi antibodies were measured by enzyme-linked immunosorbent assay (ELISA).	
End point type	Secondary
End point timeframe:	
Day 28 post-vaccination	

End point values	Adults (Group 1)	Adolescents (Group 2)	Children (Group 3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	7	5	
Units: Titer ratios (1/dil)				
geometric mean (confidence interval 95%)				
GMTRs of Antibodies to Vi Antibody	22.6 (19.1 to 26.8)	31.4 (9.2 to 107.9)	135.6 (82.5 to 222.8)	

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Reporting a Solicited Injection Site or Systemic Reactions Following Vaccination With a Typhoid Vi Polysaccharide Vaccine

End point title	Number of Subjects Reporting a Solicited Injection Site or Systemic Reactions Following Vaccination With a Typhoid Vi Polysaccharide Vaccine
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End point description:

Solicited injection site: Pain, Erythema, and Swelling; Solicited systemic reactions: Fever (Temperature), Headache, Malaise, Myalgia. Grade 3 Injection site (Children): Pain, Incapacitating, unable to perform usual activities; Erythema and Swelling,  $\geq 50$  mm; Grade 3 Injection site (Adolescents and Adults): Pain, Significant, prevents daily activity; Erythema and Swelling,  $> 100$  mm. Grade 3 Systemic reactions: Fever,  $\geq 39.0^{\circ}\text{C}$ ; Headache, Malaise, and Myalgia, Significant, prevents daily activity.

End point type	Secondary
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End point timeframe:

Day 0 up to Day 7 post-vaccination

End point values	Adults (Group 1)	Adolescents (Group 2)	Children (Group 3)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	7	5	
Units: Number of subjects				
number (not applicable)				
Injection site Pain	139	6	3	
Grade 3 Injection site Pain	0	0	0	
Injection site Erythema	0	0	2	
Grade 3 Injection site Erythema	0	0	0	
Injection site Swelling	1	0	0	
Grade 3 Injection site Swelling	0	0	0	
Fever	2	0	1	
Grade 3 Fever	0	0	0	
Headache	14	0	0	
Grade 3 Headache	1	0	0	
Malaise	23	0	0	
Grade 3 Malaise	2	0	0	
Myalgia	93	4	1	
Grade 3 Myalgia	2	0	0	

## 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-vaccination.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	15
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### Reporting groups

Reporting group title	Adults (Group 1)
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Reporting group description:

Subjects  $\geq 18$  years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.

Reporting group title	Adolescents (Group 2)
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Reporting group description:

Subjects 12 to 17 years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.

Reporting group title	Children (Group 3)
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Reporting group description:

Subjects 2 to 11 years of age received a single dose (0.5 mL) of Typhoid Vi Polysaccharide Vaccine.

Serious adverse events	Adults (Group 1)	Adolescents (Group 2)	Children (Group 3)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 188 (0.53%)	0 / 7 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 188 (0.53%)	0 / 7 (0.00%)	0 / 5 (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

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

Non-serious adverse events	Adults (Group 1)	Adolescents (Group 2)	Children (Group 3)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 188 (73.94%)	6 / 7 (85.71%)	3 / 5 (60.00%)
Nervous system disorders			
Headache			
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	14 / 188 (7.45%) 14	0 / 7 (0.00%) 0	0 / 5 (0.00%) 0
General disorders and administration site conditions Fever alternative assessment type: Systematic subjects affected / exposed occurrences (all)	2 / 188 (1.06%) 2	0 / 7 (0.00%) 0	1 / 5 (20.00%) 1
Injection site Erythema alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 188 (0.00%) 0	0 / 7 (0.00%) 0	2 / 5 (40.00%) 2
Injection site Pain alternative assessment type: Systematic subjects affected / exposed occurrences (all)	139 / 188 (73.94%) 139	6 / 7 (85.71%) 6	3 / 5 (60.00%) 3
Malaise alternative assessment type: Systematic subjects affected / exposed occurrences (all)	23 / 188 (12.23%) 23	0 / 7 (0.00%) 0	0 / 5 (0.00%) 0
Gastrointestinal disorders Stomatitis subjects affected / exposed occurrences (all)	1 / 188 (0.53%) 1	1 / 7 (14.29%) 1	0 / 5 (0.00%) 0
Musculoskeletal and connective tissue disorders Myalgia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	93 / 188 (49.47%) 93	4 / 7 (57.14%) 4	1 / 5 (20.00%) 1
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 188 (3.72%) 7	0 / 7 (0.00%) 0	1 / 5 (20.00%) 1

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported