

**Clinical trial results:****Safety and Immunogenicity Study for Use of Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine (Menactra®) versus Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Adacel®) in Subjects 11 to 55 Years of Age in South Korea****Summary**

EudraCT number	2015-005181-33
Trial protocol	Outside EU/EEA
Global end of trial date	17 January 2013

**Results information**

Result version number	v1 (current)
This version publication date	14 February 2016
First version publication date	14 February 2016

**Trial information****Trial identification**

Sponsor protocol code	MTA52
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01642589
WHO universal trial number (UTN)	U1111-1122-2028

Notes:

**Sponsors**

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon Cedex 07, France, F-69367
Public contact	Medical Product Leader, Sanofi Pasteur SA, 33 4 37 65 96 18, Philipp.oster@sanofipasteur.com
Scientific contact	Medical Product Leader, Sanofi Pasteur SA, 33 4 37 65 96 18, Philipp.oster@sanofipasteur.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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	19 April 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	17 January 2013
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

To demonstrate that the seroconversion rate is higher than 60% for serogroups A, C, Y and W-135, 28 days after a single dose of Menactra® (Group 1)

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

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Korea, Republic of: 300
Worldwide total number of subjects	300
EEA total number of subjects	0

Notes:

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**Subjects enrolled per age group**

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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)	33
Adolescents (12-17 years)	116
Adults (18-64 years)	151

From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study subjects were enrolled from 13 July 2012 to 17 December 2012 in 8 clinic centers in South Korea.

### Pre-assignment

Screening details:

A total of 300 subjects that met all inclusion but none of the exclusion criteria were randomized and vaccinated in this study.

### 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, Monitor, Assessor

Blinding implementation details:

The investigator (blind observer/assessor) and subject's parents/guardians did not know the vaccine administered. The blind-observer Investigator was in charge of safety assessment in a separate room away from where the vaccines were prepared. The vaccinator was in charge of the preparation and administration of the vaccine(s) in another room away from the blind-observer Investigator. When necessary the scratch off emergency decoding procedure described in the study protocol were to be followed.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Menactra® Group

Arm description:

Subjects received Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine (Menactra®)

Arm type	Experimental
Investigational medicinal product name	Meningococcal A/C/Y/W-135 Conjugated Polysaccharide Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection on Day 0

<b>Arm title</b>	Tdap-Adacel® Group
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Arm description:

Subjects received Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap-Adacel®).

Arm type	Active comparator
Investigational medicinal product name	Tdap vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection on Day 0

<b>Number of subjects in period 1</b>	Menactra® Group	Tdap-Adacel® Group
Started	200	100
Completed	199	99
Not completed	1	1
Consent withdrawn by subject	1	1

## Baseline characteristics

### Reporting groups

Reporting group title	Menactra® Group
Reporting group description: Subjects received Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine (Menactra®)	
Reporting group title	Tdap-Adacel® Group
Reporting group description: Subjects received Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap-Adacel®).	

Reporting group values	Menactra® Group	Tdap-Adacel® Group	Total
Number of subjects	200	100	300
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)	24	9	33
Adolescents (12-17 years)	76	40	116
Adults (18-64 years)	100	51	151
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	24.9	24.2	-
standard deviation	± 11.5	± 10.1	-
Gender categorical			
Units: Subjects			
Female	107	58	165
Male	93	42	135

## End points

### End points reporting groups

Reporting group title	Menactra® Group
Reporting group description: Subjects received Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine (Menactra®)	
Reporting group title	Tdap-Adacel® Group
Reporting group description: Subjects received Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap-Adacel®).	

### Primary: Percentage of Subjects with Seroconversion Following Vaccination With Either Menactra® or Adacel® Vaccine

End point title	Percentage of Subjects with Seroconversion Following Vaccination With Either Menactra® or Adacel® Vaccine <sup>[1]</sup>
End point description: Functional antibody activity for anti-meningococcal antibody to serogroups A, C, Y, and W-135 were measured using the Serum bactericidal assay using baby rabbit complement (SBA-BR). Seroconversion was defined as post-vaccination antibody titers of $\geq 4$ -fold increase from pre-vaccination level.	
End point type	Primary
End point timeframe: 28 days 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	Menactra® Group	Tdap-Adacel® Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	100		
Units: Percentage of subjects				
number (not applicable)				
Serogroup A	78	9		
Serogroup C	88	8		
Serogroup Y	75	12		
Serogroup W-135	92	8		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects with Functional Antibody Titers at $\geq 1:8$ Dilution Before and After Menactra® or Adacel® Vaccination

End point title	Percentage of Subjects with Functional Antibody Titers at $\geq 1:8$ Dilution Before and After Menactra® or Adacel® Vaccination
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End point description:

Functional antibody activity for anti-meningococcal antibody to serogroups A, C, Y, and W-135 were measured using the Serum bactericidal assay using baby rabbit complement (SBA-BR) at  $\geq 1:8$  dilution.

End point type Secondary

End point timeframe:

Day 0 (pre-vaccination) and 28 days post-vaccination

<b>End point values</b>	Menactra® Group	Tdap-Adacel® Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	100		
Units: Percentage of subjects number (not applicable)				
Serogroup A (Pre-vaccination)	68	76		
Serogroup A (Post-vaccination)	100	78		
Serogroup C (Pre-vaccination)	28	19		
Serogroup C (Post-vaccination)	93	24		
Serogroup Y (Pre-vaccination)	75	75		
Serogroup Y (Post-vaccination)	99	81		
Serogroup W-135 (Pre-vaccination)	50	44		
Serogroup W-135 (Post-vaccination)	98	48		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Functional Antibody Titers at $\geq 1:128$ Dilution Before and After Menactra® or Adacel® Vaccination

End point title Percentage of Subjects With Functional Antibody Titers at  $\geq 1:128$  Dilution Before and After Menactra® or Adacel® Vaccination

End point description:

Functional antibody activity for anti-meningococcal antibody to serogroups A, C, Y, and W-135 were measured using the Serum bactericidal assay using baby rabbit complement (SBA-BR) at  $\geq 1:128$  dilution.

End point type Secondary

End point timeframe:

Day 0 (pre-vaccination) and 28 days post-vaccination

<b>End point values</b>	Menactra® Group	Tdap-Adacel® Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	100		
Units: Percentage of subjects number (not applicable)				
Serogroup A (Pre-vaccination)	57	64		

Serogroup A (Post-vaccination)	99	70		
Serogroup C (Pre-vaccination)	25	15		
Serogroup C (Post-vaccination)	89	16		
Serogroup Y (Pre-vaccination)	52	48		
Serogroup Y (Post-vaccination)	96	57		
Serogroup W-135 (Pre-vaccination)	22	25		
Serogroup W-135 (Post-vaccination)	95	27		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Geometric Mean Titers of Serum Bactericidal Assay Using Baby Rabbit Complement (SBA-BR) Antibody Against Serogroups A, C, Y, and W-135 Before and After Menactra® or Adacel® Vaccination

End point title	Geometric Mean Titers of Serum Bactericidal Assay Using Baby Rabbit Complement (SBA-BR) Antibody Against Serogroups A, C, Y, and W-135 Before and After Menactra® or Adacel® Vaccination
End point description:	Functional antibody activity for anti-meningococcal antibody to serogroups A, C, Y, and W-135 were measured using the Serum bactericidal assay using baby rabbit complement (SBA-BR).
End point type	Secondary
End point timeframe:	Day 0 (pre-vaccination) and 28 days post-vaccination

End point values	Menactra® Group	Tdap-Adacel® Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	100		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Serogroup A (pre-vaccination)	46.1 (33.7 to 63.2)	75.6 (48.9 to 117)		
Serogroup A (post-vaccination)	1121 (949 to 1324)	87.6 (57.1 to 135)		
Serogroup C (pre-vaccination)	5.8 (4.5 to 7.46)	4.63 (3.26 to 6.56)		
Serogroup C (post-vaccination)	667 (504 to 884)	5.64 (3.82 to 8.32)		
Serotype Y (pre-vaccination)	50.1 (37.7 to 66.6)	47.2 (31.9 to 69.8)		
Serotype Y (post-vaccination)	620 (521 to 738)	66.8 (45.5 to 98)		
Serotype W-135 (pre-vaccination)	13 (9.83 to 17.1)	11.9 (7.79 to 18.1)		
Serotype W-135 (post-vaccination)	851 (690 to 1050)	14.9 (9.5 to 23.4)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Reporting Solicited Injection Site and Systemic Events Following Vaccination With Either Menactra® or Adacel® Vaccine

End point title	Number of Subjects Reporting Solicited Injection Site and Systemic Events Following Vaccination With Either Menactra® or Adacel® Vaccine
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End point description:

Solicited injection site reactions: Pain, Erythema, and Swelling. Solicited systemic reactions: Fever (Temperature), Headache, Malaise, Myalgia.

Grade 3 injection site reactions: Pain – Significant, prevents daily activity; Erythema and Swelling – >100 mm. Grade 3 sytemic reactions: Fever –  $\geq 39.0^{\circ}\text{C}$ ; Headache, Malaise, Myalgia – Significant, prevents daily activity.

End point type	Secondary
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End point timeframe:

Day 0 up to Day 28 post-vaccination

End point values	Menactra® Group	Tdap-Adacel® Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	100		
Units: Number of subjects				
number (not applicable)				
Injection site Pain	64	72		
Grade 3 Injection site Pain	1	2		
Injection site Erythema	5	9		
Grade 3 Injection site Erythema	0	0		
Injection site Swelling	3	6		
Grade 3 Injection site Swelling	0	0		
Fever	0	3		
Grade 3 Fever	0	0		
Headache	37	24		
Grade 3 Headache	2	1		
Malaise	36	23		
Grade 3 Malaise	1	1		
Myalgia	51	42		
Grade 3 Myalgia	1	1		

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events 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	14
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### Reporting groups

Reporting group title	Menactra® Group
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Reporting group description:

Subjects received Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine (Menactra®)

Reporting group title	Tdap-Adacel® Group
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Reporting group description:

Subjects received Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap-Adacel®).

<b>Serious adverse events</b>	Menactra® Group	Tdap-Adacel® Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 200 (0.00%)	0 / 100 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

<b>Non-serious adverse events</b>	Menactra® Group	Tdap-Adacel® Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	92 / 200 (46.00%)	76 / 100 (76.00%)	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[1]</sup>	37 / 199 (18.59%)	24 / 99 (24.24%)	
occurrences (all)	37	24	
General disorders and administration site conditions			
Injection site Pain			
alternative assessment type: Systematic			

subjects affected / exposed <sup>[2]</sup>	64 / 199 (32.16%)	72 / 99 (72.73%)	
occurrences (all)	64	72	
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[3]</sup>	5 / 199 (2.51%)	9 / 99 (9.09%)	
occurrences (all)	5	9	
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[4]</sup>	3 / 199 (1.51%)	6 / 99 (6.06%)	
occurrences (all)	3	6	
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[5]</sup>	36 / 199 (18.09%)	23 / 99 (23.23%)	
occurrences (all)	36	23	
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[6]</sup>	51 / 199 (25.63%)	42 / 99 (42.42%)	
occurrences (all)	51	42	

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 7 days after 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 7 days after 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 7 days after 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 7 days after 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 7 days after 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.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects

exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited adverse event recorded in a diary card within 7 days after 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? Yes

Date	Amendment
06 February 2012	Lowered the age of eligible subjects from 12 to 11 years in order to align with US data, clarified that the calculation for the seroconversion rate would be for the overall population, updated the exclusion criteria, and clarified the type of influenza vaccine to be used.
23 February 2012	Study exclusion criteria were further clarified.
30 March 2012	As per the Korean Food and Drug Administration, the exclusion criteria were modified such that the language that permitted inactivated influenza vaccine to be given within 2 weeks before or after vaccination was removed.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported