



## Clinical trial results: Immunogenicity and Safety of the Trivalent Influenza Vaccine (Split-Virion, Inactivated), Northern Hemisphere 2013-2014 Formulation (Intradermal Route)

### Summary

EudraCT number	2012-005243-25
Trial protocol	FR
Global end of trial date	30 July 2013

### Results information

Result version number	v1 (current)
This version publication date	10 February 2016
First version publication date	03 December 2014

### Trial information

#### Trial identification

Sponsor protocol code	GID37
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1127-7490

Notes:

### Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	1541, Avenue Marcel Mérieux, Marcy L'Etoile, France, 69280
Public contact	Medical Franchise Leader, Sanofi Pasteur SA, +33 (0)4 37 37 70 82 , eric.desauziers@sanofipasteur.com
Scientific contact	Medical Franchise Leader, Sanofi Pasteur SA, +33 (0)4 37 37 70 82 , eric.desauziers@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?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 August 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	30 July 2013
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

- To evaluate the compliance, in terms of immunogenicity, of the ID influenza vaccine NH 2013-2014 formulation with the requirements of the Committee for Medicinal Products for Human Use (CHMP) Note for Guidance (NfG) CPMP/BWP/214/96 in both age groups
- To describe the safety of the ID influenza vaccine NH 2013-2014 formulation in both age groups

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were 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 were also available on site in case of any immediate allergic reactions.

Background therapy:

The new formulation of the trivalent ID influenza vaccine for the 2013-2014 season in the Northern Hemisphere was evaluated in compliance with the Committee for Medicinal Products for Human Use (CHMP) Note for Guidance (NfG) on harmonization of requirements for influenza vaccines CPMP/BWP/214/96.

Evidence for comparator:

Not applicable

Actual start date of recruitment	03 July 2013
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	France: 130
Worldwide total number of subjects	130
EEA total number of subjects	130

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	96
From 65 to 84 years	34
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Study subjects were enrolled from 03 July 2013 to 10 July 2013 in 2 clinic centers in France.

### Pre-assignment

Screening details:

A total of 130 subjects who met all 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	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	18 to 59 years (9 µg)
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Arm description:

Subjects aged 18 to 59 years who were vaccinated with one dose of the intradermal (ID) influenza vaccine 9 µg, Northern Hemisphere (NH) 2013-2014 formulation.

Arm type	Experimental
Investigational medicinal product name	IDflu 9µg
Investigational medicinal product code	415
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

0.1 mL, intradermal into the deltoid muscle area, one dose on Day 0

<b>Arm title</b>	60 years or older (15 µg)
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Arm description:

Subjects aged 60 years or older who were vaccinated with one dose of the intradermal (ID) influenza vaccine 15 µg, NH 2013-2014 formulation.

Arm type	Experimental
Investigational medicinal product name	IDflu 15µg
Investigational medicinal product code	416
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

0.1 mL, intradermal into the deltoid muscle area, one dose on Day 0

<b>Number of subjects in period 1</b>	18 to 59 years (9 µg)	60 years or older (15 µg)
Started	65	65
Completed	65	65

## Baseline characteristics

### Reporting groups

Reporting group title	18 to 59 years (9 µg)
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Reporting group description:

Subjects aged 18 to 59 years who were vaccinated with one dose of the intradermal (ID) influenza vaccine 9 µg, Northern Hemisphere (NH) 2013-2014 formulation.

Reporting group title	60 years or older (15 µg)
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Reporting group description:

Subjects aged 60 years or older who were vaccinated with one dose of the intradermal (ID) influenza vaccine 15 µg, NH 2013-2014 formulation.

Reporting group values	18 to 59 years (9 µg)	60 years or older (15 µg)	Total
Number of subjects	65	65	130
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	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	65	31	96
From 65-84 years	0	34	34
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	41.7	67.1	
standard deviation	± 12.6	± 5.5	-
Gender categorical			
Units: Subjects			
Female	35	37	72
Male	30	28	58
Seasonal flu vaccination NH 2012-2013			
Units: Subjects			
Yes	11	23	34
No	54	42	96
Unknown	0	0	0
History of influenza diagnosis in the previous year			
Units: Subjects			
Yes	1	0	1
No	64	65	129
Unknown	0	0	0

## End points

### End points reporting groups

Reporting group title	18 to 59 years (9 µg)
Reporting group description: Subjects aged 18 to 59 years who were vaccinated with one dose of the intradermal (ID) influenza vaccine 9 µg, Northern Hemisphere (NH) 2013-2014 formulation.	
Reporting group title	60 years or older (15 µg)
Reporting group description: Subjects aged 60 years or older who were vaccinated with one dose of the intradermal (ID) influenza vaccine 15 µg, NH 2013-2014 formulation.	

### Primary: Geometric Mean Titers (GMTs) of influenza Vaccine Antibodies Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route

End point title	Geometric Mean Titers (GMTs) of influenza Vaccine Antibodies Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route <sup>[1]</sup>
End point description: Antibodies against influenza vaccine were evaluated using the hemagglutination inhibition technique.	
End point type	Primary
End point timeframe: Day 0 (pre-vaccination) and Day 21 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	18 to 59 years (9 µg)	60 years or older (15 µg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	65		
Units: Titers				
geometric mean (confidence interval 95%)				
A/California/07/2009 (H1N1; Day 0)	52.2 (35.2 to 77.6)	21.2 (14.7 to 30.7)		
A/Texas/50/2012 (H3N2; Day 0)	48.2 (32.6 to 71.4)	47.4 (31.6 to 71.3)		
B/Massachusetts/02/2012 (Day 0)	164 (118 to 230)	85.3 (61 to 119)		
A/California/07/2009 (H1N1; Day 21)	467 (356 to 613)	240 (164 to 351)		
A/Texas/50/2012 (H3N2; Day 21)	708 (511 to 981)	585 (406 to 843)		
B/Massachusetts/02/2012 (Day 21)	1233 (959 to 1586)	572 (446 to 733)		

## Statistical analyses

No statistical analyses for this end point

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**Primary: Percentage of Subjects with Seroprotection Against Influenza Vaccine Antigens Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route**

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End point title	Percentage of Subjects with Seroprotection Against Influenza Vaccine Antigens Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route <sup>[2]</sup>
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End point description:

Antibodies against influenza vaccine were evaluated using the hemagglutination inhibition technique. Seroprotection was defined as titer  $\geq 40$  (1/dilution [1/dil]) on Day 0 and Day 21.

End point type	Primary
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End point timeframe:

Day 0 (pre-vaccination) and Day 21 post-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	18 to 59 years (9 µg)	60 years or older (15 µg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	65		
Units: Percentage of subjects				
number (not applicable)				
A/California/07/2009 (H1N1; Day 0)	64.6	35.4		
A/Texas/50/2012 (H3N2; Day 0)	56.9	58.5		
B/Massachusetts/02/2012 (Day 0)	87.7	78.5		
A/California/07/2009 (H1N1; Day 21)	95.4	87.7		
A/Texas/50/2012 (H3N2; Day 21)	98.5	98.5		
B/Massachusetts/02/2012 (Day 21)	100	100		

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**Statistical analyses**

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No statistical analyses for this end point

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**Primary: Summary of Geometric Mean Titer Ratios (GMTRs) of Influenza Vaccine Antibodies After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route**

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End point title	Summary of Geometric Mean Titer Ratios (GMTRs) of Influenza Vaccine Antibodies After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route <sup>[3]</sup>
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End point description:

Antibodies against influenza vaccine were evaluated using the hemagglutination inhibition technique. Geometric mean titer ratio is the geometric mean of the individual post-vaccination/pre-vaccination titer of antibodies to the influenza vaccine.

End point type	Primary
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End point timeframe:

Day 0 (pre-vaccination) and Day 21 post-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	18 to 59 years (9 µg)	60 years or older (15 µg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	65		
Units: Titer ratios				
geometric mean (confidence interval 95%)				
A/California/07/2009 (H1N1)	8.95 (6.02 to 13.3)	11.3 (7.2 to 17.8)		
A/Texas/50/2012 (H3N2)	14.7 (9.6 to 22.5)	12.3 (7.82 to 19.4)		
B/Massachusetts/02/2012	7.5 (5.38 to 10.5)	6.71 (4.68 to 9.62)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Subjects Achieving Seroconversion or Significant Increase in Influenza Vaccine Antibodies Following Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route

End point title	Percentage of Subjects Achieving Seroconversion or Significant Increase in Influenza Vaccine Antibodies Following Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route <sup>[4]</sup>
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End point description:

Seroconversion was defined as percentage of subjects with a pre-vaccination titer < 10 (1/dil) to a post-vaccination titer ≥ 40 (1/dil) ; Significant increase was defined as the percentage of subjects with a pre-vaccination titer ≥ 10 (1/dil) and ≥ 4-fold increase of the titer.

End point type	Primary
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End point timeframe:

Day 21 post-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	18 to 59 years (9 µg)	60 years or older (15 µg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	65		
Units: Percentage				
number (not applicable)				
A/California/07/2009 (H1N1)	61.5	61.5		
A/Texas/50/2012 (H3N2)	76.9	72.3		
B/Massachusetts/02/2012	61.5	63.1		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects Reporting Solicited Injection Site or Systemic Reactions Following Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route

End point title	Percentage of Subjects Reporting Solicited Injection Site or Systemic Reactions Following Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route
End point description:	
Solicited Injection Site Reactions: Injection site Pain, Injection site Erythema, Injection site Swelling, Injection site Induration, Injection site Ecchymosis, and Injection site Pruritus. Solicited Systemic Reactions: Fever, Headache, Malaise, Myalgia, and Shivering. Grade 3 Solicited Injection Site Reactions: Injection site Pain and Pruritus, Significant, prevents daily activity; Injection site Erythema, Swelling, Induration, and Ecchymosis, >100 mm. Grade 3 Solicited Systemic Reactions: Fever, $\geq 39^{\circ}\text{C}$ , Headache, Malaise, Myalgia, and Shivering, Significant prevents daily activity.	
End point type	Secondary
End point timeframe:	
Day 0 up to Day 7 post-vaccination	

End point values	18 to 59 years (9 µg)	60 years or older (15 µg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	65		
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	33.8	20		
Grade 3 Injection site Pain	0	0		
Injection site Erythema	35.4	41.5		
Grade 3 Injection site Erythema	0	0		
Injection site Swelling	7.7	7.7		
Grade 3 Injection site Swelling	0	0		
Injection site Induration	7.7	6.2		
Grade 3 Injection site Induration	0	0		
Injection site Ecchymosis	0	0		
Grade 3 Injection site Ecchymosis	0	0		
Injection site Pruritus	29.2	33.8		
Grade 3 Injection site Pruritus	0	0		
Fever	1.5	0		
Grade 3 Fever	0	0		
Headache	24.6	9.2		
Grade 3 Headache	1.5	0		
Malaise	9.2	4.6		

Grade 3 Malaise	0	0		
Myalgia	23.1	9.2		
Grade 3 Myalgia	0	0		
Shivering	6.2	1.5		
Grade 3 Shivering	0	0		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Summary of Solicited Reactions Listed in the CHMP Note for Guidance Within 3 days after Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route

End point title	Summary of Solicited Reactions Listed in the CHMP Note for Guidance Within 3 days after Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route
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End point description:

Solicited Injection Site Reactions: Injection site Pain, Injection site Erythema, Injection site Swelling, Injection site Induration, Injection site Ecchymosis, and Injection site Pruritus. Solicited Systemic Reactions: Fever, Headache, Malaise, Myalgia, and Shivering.

End point type	Secondary
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End point timeframe:

Day 0 up to Day 3 post-vaccination

End point values	18 to 59 years (9 µg)	60 years or older (15 µg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	65		
Units: Percentage of subjects				
number (not applicable)				
Injection site Induration (≥50 mm for 4 days)	0	0		
Injection site Ecchymosis/Injection site Bruising	0	1.5		
Pyrexia (>38°C) for at least 1 day	1.5	0		
Malaise	7.7	3.1		
Shivering (Rigors)	6.2	1.5		

## 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 21 post-vaccination.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.0
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### Reporting groups

Reporting group title	18 to 59 years (9 µg)
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Reporting group description:

Subjects aged 18 to 59 years who were vaccinated with one dose of the intradermal (ID) influenza vaccine 9 µg, Northern Hemisphere (NH) 2013-2014 formulation.

Reporting group title	60 years or older (15 µg)
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Reporting group description:

Subjects aged 60 years or older who were vaccinated with one dose of the intradermal (ID) influenza vaccine 15 µg, Northern Hemisphere (NH) 2013-2014 formulation.

<b>Serious adverse events</b>	18 to 59 years (9 µg)	60 years or older (15 µg)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 65 (0.00%)	0 / 65 (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>	18 to 59 years (9 µg)	60 years or older (15 µg)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 65 (35.38%)	27 / 65 (41.54%)	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 65 (24.62%)	6 / 65 (9.23%)	
occurrences (all)	16	6	
General disorders and administration site conditions			
Injection site pain			
alternative assessment type: Systematic			

subjects affected / exposed	22 / 65 (33.85%)	13 / 65 (20.00%)	
occurrences (all)	22	13	
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 65 (35.38%)	27 / 65 (41.54%)	
occurrences (all)	23	27	
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 65 (7.69%)	5 / 65 (7.69%)	
occurrences (all)	5	5	
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 65 (7.69%)	4 / 65 (6.15%)	
occurrences (all)	5	4	
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 65 (9.23%)	3 / 65 (4.62%)	
occurrences (all)	6	3	
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 65 (6.15%)	1 / 65 (1.54%)	
occurrences (all)	4	1	
Skin and subcutaneous tissue disorders			
Injection site pruritus			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 65 (29.23%)	22 / 65 (33.85%)	
occurrences (all)	19	22	
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 65 (23.08%)	6 / 65 (9.23%)	
occurrences (all)	15	6	

## **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