Clinical trial results:
Immunogenicity and Safety of the Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation (Intradermal Route)

Summary

EudraCT number	2009-009977-85
Trial protocol	FR
Global end of trial date	18 June 2009

Results information

Result version number	v1 (current)
This version publication date	05 February 2016
First version publication date	29 January 2015

Trial information

Trial identification

Sponsor protocol code	GID29

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00945438
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 (4) 37 37 5850, Stephanie.pepin@sanofipasteur.com
Scientific contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (4) 37 37 5850, Stephanie.pepin@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	08 September 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 June 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

In subjects aged 18 to 59 years for the intradermal (ID) influenza vaccine 9 µg and in subjects aged 60 years or older for the ID influenza vaccine 15 µg:

1) To evaluate compliance, in terms of immunogenicity, of the corresponding strength of the ID influenza vaccine Northern Hemisphere (NH) 2009-2010 formulation with the requirements of the Committee for Proprietary Medicinal Products (CPMP) Note for Guidance (NfG) CPMP/BWP/214/96.

2) To describe the safety of the corresponding strength of the ID influenza vaccine, NH 2009-2010 formulation.

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 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	28 May 2009
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: 131
Worldwide total number of subjects	131
EEA total number of subjects	131

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)	80
From 65 to 84 years	51
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled on 28 May 2009 in 4 clinical centers in France.

Pre-assignment

Screening details:

A total of 131 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
Arm title	18 to 59 years 9 µg

Arm description:

Subjects aged 18 to 59 years who were vaccinated on Day 0 with the intradermal (ID) influenza vaccine 9 µg, NH 2009-2010 formulation.

Arm type	Experimental
Investigational medicinal product name	ID influenza vaccine (split virion, inactivated), NH 2009-2010 formulation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

0.1 mL (9 µg strength), intradermal in the region of the deltoid muscle, one dose on Day 0.

Arm title	60 years or older 15 µg

Arm description:

Subjects aged 60 years or older who were vaccinated on Day 0 with the intradermal (ID) influenza vaccine 15 µg, NH 2009-2010 formulation.

Arm type	Experimental
Investigational medicinal product name	ID influenza vaccine (split virion, inactivated), NH 2009-2010 formulation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

0.1 mL (15 µg strength), intradermal in the region of the deltoid muscle, one dose on Day 0.

Number of subjects in period 1	18 to 59 years 9 µg	60 years or older 15 µg
Started	66	65
Completed	65	65
Not completed	1	0
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	18 to 59 years 9 µg
Reporting group description:	
Subjects aged 18 to 59 years who were vaccinated on Day 0 with the intradermal (ID) influenza vaccine 9 µg, NH 2009-2010 formulation.	
Reporting group title	60 years or older 15 µg
Reporting group description:	
Subjects aged 60 years or older who were vaccinated on Day 0 with the intradermal (ID) influenza vaccine 15 µg, NH 2009-2010 formulation.	

Reporting group values	18 to 59 years 9 µg	60 years or older 15 µg	Total
Number of subjects	66	65	131
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)	66	14	80
From 65-84 years	0	51	51
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	45.3	72.7	
standard deviation	± 11.6	± 8.3	-
Gender categorical Units: Subjects			
Female	43	39	82
Male	23	26	49
Previous influenza vaccination Units: Subjects			
Yes	37	60	97
No	28	5	33
Unknown	1	0	1
Previous influenza infection last winter Units: Subjects			
Yes	13	0	13
No	53	65	118
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 on Day 0 with the intradermal (ID) influenza vaccine 9 µg, NH 2009-2010 formulation.	
Reporting group title	60 years or older 15 µg
Reporting group description:	
Subjects aged 60 years or older who were vaccinated on Day 0 with the intradermal (ID) influenza vaccine 15 µg, NH 2009-2010 formulation.	

Primary: Summary of Geometric Mean Titers (GMTs) of Influenza Antibodies Before and After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route

End point title	Summary of Geometric Mean Titers (GMTs) of Influenza Antibodies Before and After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route[1]
End point description:	
Influenza vaccine antibodies were assessed using the hemagglutination inhibition (HAI) 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	64	64		
Units: Titers				
geometric mean (confidence interval 95%)				
Strain A/Brisbane/59/2007 (H1N1) like; Day 0	16 (11.7 to 21.9)	26.2 (19.9 to 34.6)		
Strain A/Brisbane/10/2007 (H3N2) like; Day 0	19.7 (14.4 to 26.9)	45.3 (30.4 to 67.6)		
Strain B/Brisbane/60/2008 like; Day 0	8.32 (7.07 to 9.79)	11.1 (8.94 to 13.7)		
Strain A/Brisbane/59/2007 (H1N1) like; Day 21	127 (92.1 to 174)	62 (48.6 to 79.1)		
Strain A/Brisbane/10/2007 (H3N2) like; Day 21	199 (139 to 284)	119 (82.7 to 171)		
Strain B/Brisbane/60/2008 like; Day 21	30.2 (22.8 to 39.9)	19.8 (15.8 to 24.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Seroprotection Against Influenza Antigens Before and After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route

End point title	Percentage of Subjects With Seroprotection Against Influenza Antigens Before and After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route[2]

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination Inhibition (HAI) technique. Seroprotection was defined as antibody titers ≥40 (1/dilution [1/dil]) on Day 0 and Day 21.

End point type	Primary

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	64	64		
Units: Percentage of subjects				
number (not applicable)				
Strain A/Brisbane/59/2007 (H1N1) like; Day 0	29.7	42.2		
Strain A/Brisbane/10/2007 (H3N2) like; Day 0	31.3	51.6		
Strain B/Brisbane/60/2008 like; Day 0	3.1	12.5		
Strain A/Brisbane/59/2007 (H1N1) like; Day 21	89.1	71.9		
Strain A/Brisbane/10/2007 (H3N2) like; Day 21	87.5	79.7		
Strain B/Brisbane/60/2008 like; Day 21	40.6	25		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Influenza Antibodies Titers < 10 (1/dil) Before and After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route

End point title	Percentage of Subjects With Influenza Antibodies Titers < 10 (1/dil) Before and After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route[3]

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition (HAI) technique.

End point type	Primary

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	64	64		
Units: Percentage of subjects				
number (not applicable)				
Strain A/Brisbane/59/2007 (H1N1) like; Day 0	42.2	15.6		
Strain A/Brisbane/10/2007 (H3N2) like; Day 0	34.4	18.8		
Strain B/Brisbane/60/2008 like; Day 0	68.8	56.3		
Strain A/Brisbane/59/2007 (H1N1) like; Day 21	3.1	0		
Strain A/Brisbane/10/2007 (H3N2) like; Day 21	1.6	1.6		
Strain B/Brisbane/60/2008 like; Day 21	14.1	20.3		

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Geometric Mean Titer Ratios (GMTRs) of Influenza Antibodies Before and After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route

End point title	Summary of Geometric Mean Titer Ratios (GMTRs) of Influenza Antibodies Before and After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route[4]

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition (HAI) technique. Geometric mean of individual ratio was defined as the mean geometric increase between Day 0 and Day 21.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and 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	64	64		
Units: Titer ratios				
geometric mean (confidence interval 95%)				

Strain A/Brisbane/59/2007 (H1N1) like	7.91 (5.59 to 11.2)	2.37 (1.8 to 3.11)		
Strain A/Brisbane/10/2007 (H3N2) like	10.1 (6.82 to 14.9)	2.62 (1.99 to 3.45)		
Strain B/Brisbane/60/2008 like	3.63 (2.74 to 4.8)	1.79 (1.47 to 2.16)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Achieving Seroconversion or Significant Increase Against Influenza Antigen After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route

End point title	Percentage of Subjects Achieving Seroconversion or Significant Increase Against Influenza Antigen After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route[5]

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition (HAI) technique. Seroconversion was defined as subjects with a titer <10 (1/dil) on Day 0: post-injection titer ≥40 (1/dil) on Day 21 or significant increase for subjects with a titer ≥10 (1/dil) on Day 0: ≥4-fold increase of post-injection titer on Day 21.

End point type	Primary

End point timeframe:

Day 21 post-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	18 to 59 years 9 µg	60 years or older 15 µg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	64		
Units: Percentage of subjects				
number (not applicable)				
Strain A/Brisbane/59/2007 (H1N1) like	65.6	17.2		
Strain A/Brisbane/10/2007 (H3N2) like	67.2	25		
Strain B/Brisbane/60/2008 like	34.4	4.7		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Solicited Reactions Listed in the CPMP Note for Guidance Within 3 Days After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route

End point title	Percentage of Subjects Reporting Solicited Reactions Listed in the CPMP Note for Guidance Within 3 Days After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route[6]

End point description:

Solicited injection site reactions: Injection site induration ≥5 cm for at least 4 consecutive days and Injection site ecchymosis. Solicited systemic reactions: Pyrexia (recorded temperature > 38°C) for at least one day, Malaise, and Shivering.

End point type	Primary

End point timeframe:

Day 0 up to Day 3 post-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	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)				
At least 1 reaction listed in CPMP recommendation	7.7	4.6		
Injection site induration ≥5 cm for 4 days	0	0		
Injection site ecchymosis	1.5	0		
Pyrexia (recorded temperature > 38°C) for 1 day	0	0		
Malaise	3.1	1.5		
Shivering	6.2	4.6		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction Within 3 Days After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route

End point title	Percentage of Subjects Reporting Solicited Injection-site or Systemic Reaction Within 3 Days After Vaccination with Influenza Vaccine (Split Virion, Inactivated), Northern Hemisphere 2009-2010 Formulation Administered by Intradermal Route[7]

End point description:

Solicited injection site reactions: Pain, Erythema, Swelling, Induration, Ecchymosis, and Pruritus. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Shivering. Grade 3 Solicited injection site reactions: Pain and Pruritus – Significant, prevents daily activity; Erythema, Swelling, Induration, and Ecchymosis - >10 cm. Grade 3 systemic reactions: Fever - ≥39.0°C; Headache, Malaise, Myalgia, and Shivering – Significant, prevents daily activity.

End point type	Primary

End point timeframe:

Day 0 up to Day 3 post-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	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	55.4	16.9		
Grade 3 Injection site Pain	0	0		
Injection site Erythema	40	32.3		
Grade 3 Injection site Erythema	0	0		
Injection site Swelling	10.8	6.2		
Grade 3 Injection site Swelling	0	0		
Injection site Induration	10.8	3.1		
Grade 3 Injection site Induration	0	0		
Injection site Ecchymosis	0	0		
Grade 3 Injection site Ecchymosis	0	0		
Injection site Pruritus	32.3	24.6		
Grade 3 Injection site Pruritus	0	0		
Fever	0	0		
Grade 3 Fever	0	0		
Headache	7.7	7.7		
Grade 3 Headache	0	0		
Malaise	3.1	1.5		
Grade 3 Malaise	0	0		
Myalgia	12.3	7.7		
Grade 3 Myalgia	0	0		
Shivering	6.2	4.6		
Grade 3 Shivering	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 21 post-vaccination.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups	
Reporting group title	18 to 59 years 9 µg
Reporting group description:	
Subjects aged 18 to 59 years who were vaccinated on Day 0 with the intradermal (ID) influenza vaccine 9 µg, NH 2009-2010 formulation.	
Reporting group title	60 years or older 15 µg
Reporting group description:	
Subjects aged 60 years or older who were vaccinated on Day 0 with the intradermal (ID) influenza vaccine 15 µg, NH 2009-2010 formulation.	

Serious adverse events	18 to 59 years 9 µg	60 years or older 15 µg	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 65 (1.54%)	0 / 65 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	1 / 65 (1.54%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	18 to 59 years 9 µg	60 years or older 15 µg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 65 (55.38%)	21 / 65 (32.31%)	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			

subjects affected / exposed	5 / 65 (7.69%)	5 / 65 (7.69%)	
occurrences (all)	5	5	
General disorders and administration site conditions			
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	36 / 65 (55.38%)	11 / 65 (16.92%)	
occurrences (all)	36	11	
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	26 / 65 (40.00%)	21 / 65 (32.31%)	
occurrences (all)	26	21	
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 65 (10.77%)	4 / 65 (6.15%)	
occurrences (all)	7	4	
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 65 (6.15%)	3 / 65 (4.62%)	
occurrences (all)	4	3	
Skin and subcutaneous tissue disorders			
Injection site pruritus			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 65 (32.31%)	16 / 65 (24.62%)	
occurrences (all)	21	16	
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 65 (10.77%)	2 / 65 (3.08%)	
occurrences (all)	7	2	
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 65 (12.31%)	5 / 65 (7.69%)	
occurrences (all)	8	5	

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