Clinical trial results:
Lot-to-Lot Consistency Study of the Investigational, Split-virion, Inactivated Influenza Vaccine, Administered by the Intradermal Route in Adults

Summary

EudraCT number	2006-002369-37
Trial protocol	LT ES GB
Global end of trial date	06 June 2007

Results information

Result version number	v1 (current)
This version publication date	05 February 2016
First version publication date	04 December 2014

Trial information

Trial identification

Sponsor protocol code	GID23

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00383539
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	1541, Avenue Marcel Mérieux, Marcy L'Etoile, France, 69280
Public contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (4) 37 37 58 50, stephanie.pepin@sanofipasteur.com
Scientific contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (4) 37 37 58 50, 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	30 April 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 June 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the three different industrial lots of the intradermal (ID) investigational vaccine induce an equivalent immune response.

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 were 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	11 September 2006
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	Spain: 211
Country: Number of subjects enrolled	United Kingdom: 896
Country: Number of subjects enrolled	France: 1048
Country: Number of subjects enrolled	Lithuania: 100
Worldwide total number of subjects	2255
EEA total number of subjects	2255

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)	2255
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled from 11 September 2006 to 31 October 2006 in 26 clinical centers (13 in France, 9 in United Kingdom, 3 in Spain, and 1 in Lithuania).

Pre-assignment

Screening details:

A total of 2255 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	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	ID 9 µg Lot 1

Arm description:

Subjects who received one dose of intradermal (ID) 9 µg Lot 1 investigational inactivated, split-virion influenza vaccine on Day 0.

Arm type	Experimental
Investigational medicinal product name	Intradermal Influenza Vaccine
Investigational medicinal product code	333
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

0.1 mL, intradermal into the upper arm (deltoid area), one dose on Day 0.

Arm title	ID 9 µg Lot 2

Arm description:

Subjects who received one dose of intradermal (ID) 9 µg Lot 2 investigational inactivated, split-virion influenza vaccine on Day 0.

Arm type	Experimental
Investigational medicinal product name	Intradermal Influenza Vaccine
Investigational medicinal product code	333
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

0.1 mL, intradermal into the upper arm (deltoid area), one dose on Day 0.

Arm title	ID 9 µg Lot 3

Arm description:

Subjects who received one dose of intradermal (ID) 9 µg Lot 3 investigational inactivated, split-virion influenza vaccine on Day 0.

Arm type	Experimental

Investigational medicinal product name	Intradermal Influenza Vaccine
Investigational medicinal product code	333
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

0.1 mL, intradermal into the upper arm (deltoid area), one dose on Day 0.

Arm title	IM 15 µg

Arm description:

Subjects who received one dose of intramuscular (IM) 15 µg investigational inactivated, split-virion influenza vaccine on Day 0.

Arm type	Active comparator
Investigational medicinal product name	Inactivated, split-virion, influenza vaccine
Investigational medicinal product code	
Other name	VAXIGRIP
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the upper arm (deltoid area), one dose on Day 0.

Number of subjects in period 1	ID 9 µg Lot 1	ID 9 µg Lot 2	ID 9 µg Lot 3
Started	604	596	603
Completed	596	586	594
Not completed	8	10	9
Consent withdrawn by subject	1	1	1
Lost to follow-up	4	7	6
Protocol deviation	3	2	2

Number of subjects in period 1	IM 15 µg
Started	452
Completed	443
Not completed	9
Consent withdrawn by subject	2
Lost to follow-up	5
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	ID 9 µg Lot 1
Reporting group description:	
Subjects who received one dose of intradermal (ID) 9 µg Lot 1 investigational inactivated, split-virion influenza vaccine on Day 0.	
Reporting group title	ID 9 µg Lot 2
Reporting group description:	
Subjects who received one dose of intradermal (ID) 9 µg Lot 2 investigational inactivated, split-virion influenza vaccine on Day 0.	
Reporting group title	ID 9 µg Lot 3
Reporting group description:	
Subjects who received one dose of intradermal (ID) 9 µg Lot 3 investigational inactivated, split-virion influenza vaccine on Day 0.	
Reporting group title	IM 15 µg
Reporting group description:	
Subjects who received one dose of intramuscular (IM) 15 µg investigational inactivated, split-virion influenza vaccine on Day 0.	

Reporting group values	ID 9 µg Lot 1	ID 9 µg Lot 2	ID 9 µg Lot 3
Number of subjects	604	596	603
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)	604	596	603
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	42.9	43.4	42.9
standard deviation	± 12.6	± 12.6	± 12.4
Gender categorical			
Units: Subjects			
Female	356	345	343
Male	248	251	260

Reporting group values	IM 15 µg	Total	
Number of subjects	452	2255	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	

Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	452	2255	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	42		
standard deviation	± 12	-	
Gender categorical			
Units: Subjects			
Female	268	1312	
Male	184	943	

End points

End points reporting groups

Reporting group title	ID 9 µg Lot 1
Reporting group description:	
Subjects who received one dose of intradermal (ID) 9 µg Lot 1 investigational inactivated, split-virion influenza vaccine on Day 0.	
Reporting group title	ID 9 µg Lot 2
Reporting group description:	
Subjects who received one dose of intradermal (ID) 9 µg Lot 2 investigational inactivated, split-virion influenza vaccine on Day 0.	
Reporting group title	ID 9 µg Lot 3
Reporting group description:	
Subjects who received one dose of intradermal (ID) 9 µg Lot 3 investigational inactivated, split-virion influenza vaccine on Day 0.	
Reporting group title	IM 15 µg
Reporting group description:	
Subjects who received one dose of intramuscular (IM) 15 µg investigational inactivated, split-virion influenza vaccine on Day 0.	

Primary: Geometric Mean Titers (GMTs) of Influenza Vaccine Antibodies Before and After Vaccination with One of Three Lots of 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 One of Three Lots of Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal Route
End point description:	
Influenza vaccine antibodies were assessed using the hemagglutination inhibition technique.	
End point type	Primary
End point timeframe:	
Day 0 (pre-vaccination) and Day 21 post vaccination	

End point values	ID 9 µg Lot 1	ID 9 µg Lot 2	ID 9 µg Lot 3	IM 15 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	418	418	414	452
Units: Titers				
geometric mean (confidence interval 95%)				
A/New Caledonia/20/99 (H1N1; Day 0)	18.8 (16.4 to 21.5)	20 (17.3 to 23)	19.7 (17.1 to 22.8)	0 (0 to 0)
A/Wisconsin 67/2005(H3N2; Day 0)	24.1 (20.9 to 27.8)	24.9 (21.4 to 29)	22.4 (19.5 to 25.8)	0 (0 to 0)
B/Malaysia 25/06/2004 (Day 0)	10.9 (10.1 to 11.9)	10.4 (9.62 to 11.3)	10.4 (9.56 to 11.3)	0 (0 to 0)
A/New Caledonia/20/99 (H1N1; Day 21)	186 (162 to 214)	183 (159 to 211)	176 (152 to 204)	0 (0 to 0)
A/Wisconsin 67/2005(H3N2; Day 21)	269 (236 to 307)	298 (260 to 340)	268 (234 to 308)	0 (0 to 0)

B/Malaysia 25/06/2004 (Day 21)	67.6 (61 to 74.9)	75.4 (67.4 to 84.3)	62.4 (55.8 to 69.7)	0 (0 to 0)

Statistical analyses

Statistical analysis title	Equivalence of ID Vaccine Lot 1 and Lot 2 (H1N1)

Statistical analysis description:

Equivalence among the three lots was demonstrated if all individual null hypotheses were rejected i.e. if the equivalence was demonstrated for each pair of lots and for each strain.
The global hypotheses were:
H0Global: Equivalence between the three lots is not demonstrated for at least one strain
H1Global: Equivalence between the three lots is demonstrated for all strains

Comparison groups	ID 9 µg Lot 1 v ID 9 µg Lot 2
Number of subjects included in analysis	836
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Method	Log transformation
Parameter estimate	Mean difference (final values)
Point estimate	0.006
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.065
upper limit	0.078

Notes:

[1] - The statistical methodology was based on the use of the two-sided 90% confidence interval (CI) of the differences of the means of the log10 transformed post-vaccination titers between pairs of lots. The CI for differences was calculated using normal approximation of log-transformed titers.
Equivalence between the two lots was demonstrated if, the two-sided 90% CI of the difference lies between -0.176 and 0.176.

Statistical analysis title	Equivalence of ID Vaccine Lot 1 and Lot 3 (H1N1)

Statistical analysis description:

Equivalence among the three lots was demonstrated if all individual null hypotheses were rejected i.e. if the equivalence was demonstrated for each pair of lots and for each strain.
The global hypotheses were:
H0Global: Equivalence between the three lots is not demonstrated for at least one strain
H1Global: Equivalence between the three lots is demonstrated for all strains

Comparison groups	ID 9 µg Lot 1 v ID 9 µg Lot 3
Number of subjects included in analysis	832
Analysis specification	Pre-specified
Analysis type	equivalence[2]
Method	Log transformation
Parameter estimate	Mean difference (final values)
Point estimate	0.023
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.051
upper limit	0.096

Notes:

[2] - The statistical methodology was based on the use of the two-sided 90% confidence interval (CI) of the differences of the means of the log10 transformed post-vaccination titers between pairs of lots. The CI for differences was calculated using normal approximation of log-transformed titers.
Equivalence between the two lots was demonstrated if, the two-sided 90% CI of the difference lies between -0.176 and 0.176.

Statistical analysis title	Equivalence of ID Vaccine Lot 2 and Lot 3 (H1N1)

Statistical analysis description:

Equivalence among the three lots was demonstrated if all individual null hypotheses were rejected i.e. if the equivalence was demonstrated for each pair of lots and for each strain.
The global hypotheses were:
H0Global: Equivalence between the three lots is not demonstrated for at least one strain
H1Global: Equivalence between the three lots is demonstrated for all strains

Comparison groups	ID 9 µg Lot 2 v ID 9 µg Lot 3
Number of subjects included in analysis	832
Analysis specification	Pre-specified
Analysis type	equivalence[3]
Method	Log transformation
Parameter estimate	Mean difference (final values)
Point estimate	0.017
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.057
upper limit	0.09

Notes:

[3] - The statistical methodology was based on the use of the two-sided 90% confidence interval (CI) of the differences of the means of the log10 transformed post-vaccination titers between pairs of lots. The CI for differences was calculated using normal approximation of log-transformed titers.
Equivalence between the two lots was demonstrated if, the two-sided 90% CI of the difference lies between -0.176 and 0.176.

Statistical analysis title	Equivalence of ID Vaccine Lot 1 and Lot 2 (H3N2)

Statistical analysis description:

Equivalence among the three lots was demonstrated if all individual null hypotheses were rejected i.e. if the equivalence was demonstrated for each pair of lots and for each strain.
The global hypotheses were:
H0Global: Equivalence between the three lots is not demonstrated for at least one strain
H1Global: Equivalence between the three lots is demonstrated for all strains

Comparison groups	ID 9 µg Lot 1 v ID 9 µg Lot 2
Number of subjects included in analysis	836
Analysis specification	Pre-specified
Analysis type	equivalence[4]
Method	Log transformation
Parameter estimate	Mean difference (final values)
Point estimate	-0.044
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.113
upper limit	0.025

Notes:

[4] - The statistical methodology was based on the use of the two-sided 90% confidence interval (CI) of the differences of the means of the log10 transformed post-vaccination titers between pairs of lots. The CI for differences was calculated using normal approximation of log-transformed titers.
Equivalence between the two lots was demonstrated if, the two-sided 90% CI of the difference lies between -0.176 and 0.176.

Statistical analysis title	Equivalence of ID Vaccine Lot 1 and Lot 3 (H3N2)

Statistical analysis description:

Equivalence among the three lots was demonstrated if all individual null hypotheses were rejected i.e. if the equivalence was demonstrated for each pair of lots and for each strain.
The global hypotheses were:
H0Global: Equivalence between the three lots is not demonstrated for at least one strain
H1Global: Equivalence between the three lots is demonstrated for all strains

Comparison groups	ID 9 µg Lot 3 v ID 9 µg Lot 1
Number of subjects included in analysis	832
Analysis specification	Pre-specified
Analysis type	equivalence[5]
Method	Log transformation
Parameter estimate	Mean difference (final values)
Point estimate	0.001
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.068
upper limit	0.07

Notes:

[5] - The statistical methodology was based on the use of the two-sided 90% confidence interval (CI) of the differences of the means of the log10 transformed post-vaccination titers between pairs of lots. The CI for differences was calculated using normal approximation of log-transformed titers.
Equivalence between the two lots was demonstrated if, the two-sided 90% CI of the difference lies between -0.176 and 0.176.

Statistical analysis title	Equivalence of ID Vaccine Lot 2 and Lot 3 (H3N2)

Statistical analysis description:

Equivalence among the three lots was demonstrated if all individual null hypotheses were rejected i.e. if the equivalence was demonstrated for each pair of lots and for each strain.
The global hypotheses were:
H0Global: Equivalence between the three lots is not demonstrated for at least one strain
H1Global: Equivalence between the three lots is demonstrated for all strains

Comparison groups	ID 9 µg Lot 3 v ID 9 µg Lot 2
Number of subjects included in analysis	832
Analysis specification	Pre-specified
Analysis type	equivalence[6]
Method	Log transformation
Parameter estimate	Mean difference (final values)
Point estimate	0.045
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.025
upper limit	0.115

Notes:

[6] - The statistical methodology was based on the use of the two-sided 90% confidence interval (CI) of the differences of the means of the log10 transformed post-vaccination titers between pairs of lots. The CI for differences was calculated using normal approximation of log-transformed titers.
Equivalence between the two lots was demonstrated if, the two-sided 90% CI of the difference lies between -0.176 and 0.176.

Statistical analysis title	Equivalence of ID Vaccine Lot 1 and Lot 2 (B)

Statistical analysis description:

Equivalence among the three lots was demonstrated if all individual null hypotheses were rejected i.e. if the equivalence was demonstrated for each pair of lots and for each strain.
The global hypotheses were:
H0Global: Equivalence between the three lots is not demonstrated for at least one strain
H1Global: Equivalence between the three lots is demonstrated for all strains

Comparison groups	ID 9 µg Lot 2 v ID 9 µg Lot 1
Number of subjects included in analysis	836
Analysis specification	Pre-specified
Analysis type	equivalence[7]
Method	Log transformation
Parameter estimate	Mean difference (final values)
Point estimate	-0.047
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.102
upper limit	0.008

Notes:

[7] - The statistical methodology was based on the use of the two-sided 90% confidence interval (CI) of the differences of the means of the log10 transformed post-vaccination titers between pairs of lots. The CI for differences was calculated using normal approximation of log-transformed titers.
Equivalence between the two lots was demonstrated if, the two-sided 90% CI of the difference lies between -0.176 and 0.176.

Statistical analysis title	Equivalence of ID Vaccine Lot 1 and Lot 3 (B)

Statistical analysis description:

Equivalence among the three lots was demonstrated if all individual null hypotheses were rejected i.e. if the equivalence was demonstrated for each pair of lots and for each strain.
The global hypotheses were:
H0Global: Equivalence between the three lots is not demonstrated for at least one strain
H1Global: Equivalence between the three lots is demonstrated for all strains

Comparison groups	ID 9 µg Lot 1 v ID 9 µg Lot 3
Number of subjects included in analysis	832
Analysis specification	Pre-specified
Analysis type	equivalence[8]
Method	Log transformation
Parameter estimate	Mean difference (final values)
Point estimate	0.035
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.09

Notes:

[8] - The statistical methodology was based on the use of the two-sided 90% confidence interval (CI) of the differences of the means of the log10 transformed post-vaccination titers between pairs of lots. The CI for differences was calculated using normal approximation of log-transformed titers.
Equivalence between the two lots was demonstrated if, the two-sided 90% CI of the difference lies between -0.176 and 0.176.

Statistical analysis title	Equivalence of ID Vaccine Lot 2 and Lot 3 (B)

Statistical analysis description:

Equivalence among the three lots was demonstrated if all individual null hypotheses were rejected i.e. if the equivalence was demonstrated for each pair of lots and for each strain.
The global hypotheses were:

H0Global: Equivalence between the three lots is not demonstrated for at least one strain
H1Global: Equivalence between the three lots is demonstrated for all strains

Comparison groups	ID 9 µg Lot 3 v ID 9 µg Lot 2
Number of subjects included in analysis	832
Analysis specification	Pre-specified
Analysis type	equivalence[9]
Method	Log transformation
Parameter estimate	Mean difference (final values)
Point estimate	0.082
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.025
upper limit	0.139

Notes:

[9] - The statistical methodology was based on the use of the two-sided 90% confidence interval (CI) of the differences of the means of the log10 transformed post-vaccination titers between pairs of lots. The CI for differences was calculated using normal approximation of log-transformed titers.
Equivalence between the two lots was demonstrated if, the two-sided 90% CI of the difference lies between -0.176 and 0.176.

Primary: Geometric Mean Titers (GMTs) of Influenza Vaccine Antibodies Before and After Vaccination with Either One of Three Lots of Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal or by Intramuscular Route

End point title	Geometric Mean Titers (GMTs) of Influenza Vaccine Antibodies Before and After Vaccination with Either One of Three Lots of Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal or by Intramuscular Route[10]

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition technique.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 post vaccination

Notes:

[10] - 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	ID 9 µg Lot 1	ID 9 µg Lot 2	ID 9 µg Lot 3	IM 15 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	604	596	414	421
Units: Titers				
geometric mean (confidence interval 95%)				
A/New Caledonia/20/99 (H1N1; Day 0)	0 (0 to 0)	0 (0 to 0)	19.5 (18 to 21.1)	19.2 (16.6 to 22.3)
A/Wisconsin 67/2005(H3N2; Day 0)	0 (0 to 0)	0 (0 to 0)	23.8 (21.9 to 25.8)	24.1 (20.9 to 27.9)
B/Malaysia 25/06/2004 (Day 0)	0 (0 to 0)	0 (0 to 0)	10.6 (10.1 to 11.1)	10.4 (9.65 to 11.3)
A/New Caledonia/20/99 (H1N1; Day 21)	0 (0 to 0)	0 (0 to 0)	182 (168 to 197)	187 (162 to 216)
A/Wisconsin 67/2005(H3N2; Day 21)	0 (0 to 0)	0 (0 to 0)	278 (257 to 301)	274 (244 to 309)
B/Malaysia 25/06/2004 (Day 21)	0 (0 to 0)	0 (0 to 0)	68.3 (64.1 to 72.7)	69.8 (62.7 to 77.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Seroconversion Against Each Influenza Vaccine Antigen Following Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal (1 of 3 lots) or by Intramuscular Route

End point title	Percentage of Subjects Achieving Seroconversion Against Each Influenza Vaccine Antigen Following Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal (1 of 3 lots) or by Intramuscular Route

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition technique. Seroconversion was defined as subjects with a pre-vaccination anti-HA antibody individual titer <10 (1/dil): post-vaccination anti-HA antibody individual titer ≥40 (1/dil) or significant increase in subjects with a pre-vaccination anti-HA antibody individual titer ≥10 (1/dil): ≥ four-fold increase from pre- to post-vaccination anti-HA antibody individual titer on Day 21.

End point type	Secondary

End point timeframe:

Day 21 post-vaccination

End point values	ID 9 µg Lot 1	ID 9 µg Lot 2	ID 9 µg Lot 3	IM 15 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	217	224	231	230
Units: Percentage of subjects				
number (not applicable)				
A/New Caledonia/20/99 (H1N1)	81.3	79.5	78	77.9
A/Wisconsin 67/2005 (H3N2)	84.7	86.8	88.1	90.8
B/Malaysia 25/06/2004	66.4	65.6	64.1	66.5

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Seroprotection Against Each Influenza Antigen Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal (1 of 3 lots) or Intramuscular Route

End point title	Percentage of Subjects with Seroprotection Against Each Influenza Antigen Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal (1 of 3 lots) or Intramuscular Route

End point description:

Influenza vaccine antibodies were assessed using the hemagglutination inhibition technique. Seroprotection was defined as titers ≥40 (1/dil) on Day 21.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 21 post-vaccination

End point values	ID 9 µg Lot 1	ID 9 µg Lot 2	ID 9 µg Lot 3	IM 15 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	441	428	428	436
Units: Percentage of subjects				
number (not applicable)				
A/New Caledonia/20/99 (H1N1; Day 0)	33.2	31.4	33.6	31.2
A/New Caledonia/20/99 (H1N1; Day 21)	88.2	88.1	85.3	86.2
A/Wisconsin 67/2005 (H3N2; Day 0)	38.3	38.8	36	38.1
A/Wisconsin 67/2005 (H3N2; Day 21)	92.5	94.4	93.7	95.4
B/Malaysia 25/06/2004 (B; Day 0)	11.1	10	9.9	8.5
B/Malaysia 25/06/2004 (B; Day 21)	74.3	73.4	70.9	74.8

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reporting Solicited Injection Site or Systemic Reaction Following Vaccination with One of Three Lots of Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal or by Intramuscular Route

End point title	Percentage of Subjects Reporting Solicited Injection Site or Systemic Reaction Following Vaccination with One of Three Lots of Inactivated, Split-Virion Influenza Vaccine Administered by Intradermal or by Intramuscular Route

End point description:

Solicited injection site: Pain, Erythema, Swelling, Induration, Ecchymosis, and Pruritus. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Shivering. Severe injection site: Pain and Pruritus – Incapacitating, unable to perform usual activities, may have/or required medical care or absenteeism; Erythema, Swelling, Induration, and Ecchymosis – ≥5 cm. Severe systemic reactions: Fever – >39.6°C rectal; Headache, Malaise, Myalgia, and Shivering – Prevents daily activities.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 post-vaccination

End point values	ID 9 µg Lot 1	ID 9 µg Lot 2	ID 9 µg Lot 3	IM 15 µg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	604	592	600	452
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	46.2	41.8	41.4	48.4
Severe Injection site Pain	0.2	0	0.2	0.2
Injection site Erythema	82.8	84.4	86	25.5
Severe Injection site Erythema	18.6	22.6	17.2	4.7
Injection site Swelling	61.5	62.1	62	20.7
Severe Injection site Swelling	6.9	8.2	6.9	2.7
Injection site Induration	63.4	58.5	60.5	26.1
Severe Injection site Induration	5.2	6	4.7	1.8
Injection site Ecchymosis	10.5	9.9	9.5	9.9
Severe Injection site Ecchymosis	0.5	0.7	0.7	0.7
Injection site Pruritus	45.3	44.5	44.6	13.1
Severe Injection site Pruritus	0.8	0.7	0	0.2
Fever	3.2	5	3.5	3.4
Severe Fever	0	0.3	0.2	0.4
Headache	30.3	29.5	27.7	30
Severe Headache	1.5	1.2	1.2	1.6
Malaise	18.6	18.2	17.9	19.4
Severe Malaise	2	1.2	1.9	1.6
Myalgia	23.6	22.5	24.5	29.5
Severe Myalgia	2	0.7	0.7	1.6
Shivering	10.5	8.1	9.6	7.4
Severe Shivering	1	0.5	0.2	0.9

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	7.1

Reporting groups	
Reporting group title	ID 9 µg Lot 1
Reporting group description:	
Subjects who received one dose of intradermal (ID) 9 µg Lot 1 investigational inactivated, split-virion influenza vaccine on Day 0.	
Reporting group title	ID 9 µg Lot 2
Reporting group description:	
Subjects who received one dose of intradermal (ID) 9 µg Lot 2 investigational inactivated, split-virion influenza vaccine on Day 0.	
Reporting group title	ID 9 µg Lot 3
Reporting group description:	
Subjects who received one dose of intradermal (ID) 9 µg Lot 3 investigational inactivated, split-virion influenza vaccine on Day 0.	
Reporting group title	IM 15 µg
Reporting group description:	
Subjects who received one dose of intramuscular (IM) 15 µg investigational inactivated, split-virion influenza vaccine on Day 0.	

Serious adverse events	ID 9 µg Lot 1	ID 9 µg Lot 2	ID 9 µg Lot 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 604 (0.00%)	0 / 596 (0.00%)	1 / 603 (0.17%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	0 / 604 (0.00%)	0 / 596 (0.00%)	1 / 603 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 604 (0.00%)	0 / 596 (0.00%)	0 / 603 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood and lymphatic system disorders			
Necrotising granulomatous lymphadenitis			
subjects affected / exposed	0 / 604 (0.00%)	0 / 596 (0.00%)	1 / 603 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 604 (0.00%)	0 / 596 (0.00%)	1 / 603 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 604 (0.00%)	0 / 596 (0.00%)	1 / 603 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 604 (0.00%)	0 / 596 (0.00%)	1 / 603 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 604 (0.00%)	0 / 596 (0.00%)	1 / 603 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	IM 15 µg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 452 (0.22%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	0 / 452 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 452 (0.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Necrotising granulomatous lymphadenitis			
subjects affected / exposed	0 / 452 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 452 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 452 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rotator cuff syndrome			
subjects affected / exposed	0 / 452 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 452 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ID 9 µg Lot 1	ID 9 µg Lot 2	ID 9 µg Lot 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	495 / 604 (81.95%)	493 / 596 (82.72%)	509 / 603 (84.41%)
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[1]	181 / 598 (30.27%)	172 / 583 (29.50%)	164 / 592 (27.70%)
occurrences (all)	181	172	164
General disorders and administration site conditions			
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed[2]	276 / 598 (46.15%)	244 / 584 (41.78%)	245 / 592 (41.39%)
occurrences (all)	276	244	245
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[3]	495 / 598 (82.78%)	493 / 584 (84.42%)	509 / 592 (85.98%)
occurrences (all)	495	493	509
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed[4]	368 / 598 (61.54%)	362 / 583 (62.09%)	367 / 592 (61.99%)
occurrences (all)	368	362	367
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed[5]	379 / 598 (63.38%)	341 / 583 (58.49%)	358 / 592 (60.47%)
occurrences (all)	379	341	358
Injection site ecchymosis			
alternative assessment type: Systematic			
subjects affected / exposed[6]	63 / 598 (10.54%)	58 / 583 (9.95%)	56 / 592 (9.46%)
occurrences (all)	63	58	56
Injection site pruritus			
alternative assessment type: Systematic			
subjects affected / exposed[7]	271 / 598 (45.32%)	260 / 584 (44.52%)	264 / 592 (44.59%)
occurrences (all)	271	260	264
Fever			
alternative assessment type: Systematic			

subjects affected / exposed[8]	19 / 598 (3.18%)	29 / 584 (4.97%)	21 / 592 (3.55%)
occurrences (all)	19	29	21
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed[9]	111 / 598 (18.56%)	106 / 583 (18.18%)	106 / 592 (17.91%)
occurrences (all)	111	106	106
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed[10]	63 / 598 (10.54%)	47 / 583 (8.06%)	57 / 592 (9.63%)
occurrences (all)	63	47	57
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[11]	141 / 598 (23.58%)	131 / 583 (22.47%)	145 / 592 (24.49%)
occurrences (all)	141	131	145

Non-serious adverse events	IM 15 µg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	215 / 452 (47.57%)		
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[1]	133 / 444 (29.95%)		
occurrences (all)	133		
General disorders and administration site conditions			
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed[2]	215 / 444 (48.42%)		
occurrences (all)	215		
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[3]	113 / 444 (25.45%)		
occurrences (all)	113		
Injection site swelling			
alternative assessment type: Systematic			

subjects affected / exposed[4]	92 / 444 (20.72%)		
occurrences (all)	92		
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed[5]	116 / 444 (26.13%)		
occurrences (all)	116		
Injection site ecchymosis			
alternative assessment type: Systematic			
subjects affected / exposed[6]	44 / 444 (9.91%)		
occurrences (all)	44		
Injection site pruritus			
alternative assessment type: Systematic			
subjects affected / exposed[7]	58 / 444 (13.06%)		
occurrences (all)	58		
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[8]	15 / 445 (3.37%)		
occurrences (all)	15		
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed[9]	86 / 444 (19.37%)		
occurrences (all)	86		
Shivering			
alternative assessment type: Systematic			
subjects affected / exposed[10]	33 / 444 (7.43%)		
occurrences (all)	33		
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[11]	131 / 444 (29.50%)		
occurrences (all)	131		

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 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 7 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 7 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 7 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 7 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.
[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 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.
[7] - 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 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.
[8] - 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 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.
[9] - 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 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.
[10] - 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 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.
[11] - 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 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