



Clinical trial results:

Safety of the Inactivated, Split-Virion Influenza Vaccine Administered by the Intradermal Route in Healthy Children

Summary

EudraCT number	2005-002965-35
Trial protocol	FI
Global end of trial date	02 January 2006

Results information

Result version number	v1
This version publication date	05 February 2016
First version publication date	03 December 2014

Trial information

Trial identification

Sponsor protocol code	GID18
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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 (0)4 37 37 58 50, stephanie.pepin@sanofipasteur.com
Scientific contact	Director, Clinical Development, Sanofi Pasteur SA, 33 (0)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?	Yes
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	25 September 2006
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 January 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the safety of the 9 µg formulation of the inactivated, split-virion influenza vaccine administered by the intradermal (ID) route in children aged 6 to 35 months and 3 to 8 years.

Protection of trial subjects:

Only subjects that met all of 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	26 September 2005
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	Finland: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	38
Children (2-11 years)	62
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled from 26 September 2005 to 28 October 2005 in 3 clinic centers in Finland.

Pre-assignment

Screening details:

A total of 100 subjects who met all of the 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	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
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Arm title	ID Group (Age 3–8 years)
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Arm description:

Subjects aged 3 to 8 years at enrollment who received 2 intradermal (ID) doses of the 9 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.

Arm type	Experimental
Investigational medicinal product name	Inactivated, split-virion influenza vaccine
Investigational medicinal product code	
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 each at Day 0 and Day 28

Arm title	IM Group (Age 3–8 years)
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Arm description:

Subjects aged 3 to 8 years at enrollment who received 2 intramuscular (IM) doses of the 15 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.

Arm type	Active comparator
Investigational medicinal product name	Inactivated, split-virion influenza 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 in the deltoid muscle of subjects >1 years of age, one dose each at Day 0 and Day 28

Arm title	ID Group (Age 6–35 months)
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Arm description:

Subjects age 6 to 35 months at enrollment who received 2 intradermal (ID) doses of the 9 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.

Arm type	Experimental
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Investigational medicinal product name	Inactivated, split-virion influenza vaccine
Investigational medicinal product code	
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 each at Day 0 and Day 28	
Arm title	IM Group (Age 6-35 months)

Arm description:

Subjects age 6 to 35 months at enrollment who received 2 intramuscular (IM) doses of the 7.5 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.

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

Dosage and administration details:

0.25 mL, intramuscular in the deltoid muscle of subjects >1 years of age and in the anterolateral aspect of the thigh in subjects <1 years of age, one dose each at Day 0 and Day 28.

Number of subjects in period 1	ID Group (Age 3–8 years)	IM Group (Age 3–8 years)	ID Group (Age 6-35 months)
Started	30	20	30
Completed	30	20	29
Not completed	0	0	1
Consent withdrawn by subject	-	-	1

Number of subjects in period 1	IM Group (Age 6-35 months)
Started	20
Completed	20
Not completed	0
Consent withdrawn by subject	-

Baseline characteristics

Reporting groups

Reporting group title	ID Group (Age 3–8 years)
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Reporting group description:

Subjects aged 3 to 8 years at enrollment who received 2 intradermal (ID) doses of the 9 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.

Reporting group title	IM Group (Age 3–8 years)
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Reporting group description:

Subjects aged 3 to 8 years at enrollment who received 2 intramuscular (IM) doses of the 15 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.

Reporting group title	ID Group (Age 6-35 months)
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Reporting group description:

Subjects age 6 to 35 months at enrollment who received 2 intradermal (ID) doses of the 9 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.

Reporting group title	IM Group (Age 6-35 months)
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Reporting group description:

Subjects age 6 to 35 months at enrollment who received 2 intramuscular (IM) doses of the 7.5 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.

Reporting group values	ID Group (Age 3–8 years)	IM Group (Age 3–8 years)	ID Group (Age 6-35 months)
Number of subjects	30	20	30
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	24
Children (2-11 years)	30	20	6
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: months			
arithmetic mean	58.8	49.2	13.8
standard deviation	± 1.61	± 1.04	± 7.35
Gender categorical			
Units: Subjects			
Female	10	10	17
Male	20	10	13

Reporting group values	IM Group (Age 6-35 months)	Total	
Number of subjects	20	100	
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)	14	38	
Children (2-11 years)	6	62	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: months			
arithmetic mean	15.6		
standard deviation	± 8.32	-	
Gender categorical			
Units: Subjects			
Female	12	49	
Male	8	51	

End points

End points reporting groups

Reporting group title	ID Group (Age 3–8 years)
Reporting group description: Subjects aged 3 to 8 years at enrollment who received 2 intradermal (ID) doses of the 9 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.	
Reporting group title	IM Group (Age 3–8 years)
Reporting group description: Subjects aged 3 to 8 years at enrollment who received 2 intramuscular (IM) doses of the 15 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.	
Reporting group title	ID Group (Age 6-35 months)
Reporting group description: Subjects age 6 to 35 months at enrollment who received 2 intradermal (ID) doses of the 9 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.	
Reporting group title	IM Group (Age 6-35 months)
Reporting group description: Subjects age 6 to 35 months at enrollment who received 2 intramuscular (IM) doses of the 7.5 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28.	

Primary: Percentage of Subjects Reporting Solicited Injection Site or Systemic Reaction Following Any Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or Intramuscular Route

End point title	Percentage of Subjects Reporting Solicited Injection Site or Systemic Reaction Following Any Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or Intramuscular Route ^[1]
End point description: Solicited injection site reactions (children 3–8 years): Pain, Erythema, Edema, and Induration. Solicited systemic reactions (children 3–8 years): Fever, Headache, Malaise, and Myalgia. Solicited injection site reactions (infants 6–35 months): Tenderness, Erythema, Swelling, and Induration. Solicited systemic reactions (infants 6–35 months): Fever, Vomiting, Abnormal crying, Drowsiness, Appetite loss, and Irritability.	
End point type	Primary
End point timeframe: Day 0 (pre-each vaccination) up to 7 days post-each 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	ID Group (Age 3–8 years)	IM Group (Age 3–8 years)	ID Group (Age 6-35 months)	IM Group (Age 6-35 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	63.3	65	0	0
Injection site Erythema	90	35	80	25
Injection site Edema	56.7	10	0	0
Injection site Induration	46.7	30	53.3	15
Fever	3.3	20	26.7	50

Headache	10	10	0	0
Malaise	13.3	20	0	0
Myalgia	3.3	10	0	0
Injection site Tenderness	0	0	43.3	20
Injection site Swelling	0	0	23.3	15
Vomiting	0	0	13.3	5
Abnormal crying	0	0	53.3	30
Drowsiness	0	0	43.3	15
Appetite loss	0	0	50	35
Irritability	0	0	63.3	60

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Solicited Injection Site or Systemic Reactions Within Seven Days Following the First Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or Intramuscular Route

End point title	Percentage of Subjects Reporting Solicited Injection Site or Systemic Reactions Within Seven Days Following the First Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or Intramuscular Route ^[2]
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End point description:

Solicited injection site reactions (children 3–8 years): Pain, Erythema, Edema, and Induration. Solicited systemic reactions (children 3–8 years): Fever, Headache, Malaise, and Myalgia. Solicited injection site reactions (infants 6–35 months): Tenderness, Erythema, Swelling, and Induration. Solicited systemic reactions (infants 6–35 months): Fever, Vomiting, Abnormal crying, Drowsiness, Appetite loss, and Irritability.

End point type	Primary
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End point timeframe:

Day 0 (pre-vaccination) up to 7 days post-first 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	ID Group (Age 3–8 years)	IM Group (Age 3–8 years)	ID Group (Age 6–35 months)	IM Group (Age 6–35 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	53.3	45	0	0
Injection site Erythema	66.7	20	53.3	10
Injection site Edema	26.7	10	0	0
Injection site Induration	23.3	20	13.3	5
Fever	3.3	10	23.3	40
Headache	6.7	10	0	0
Malaise	6.7	20	0	0
Myalgia	3.3	10	0	0
Injection site Tenderness	0	0	23.3	15
Injection site Swelling	0	0	10	5

Vomiting	0	0	6.7	0
Abnormal crying	0	0	33.3	15
Drowsiness	0	0	26.7	15
Appetite loss	0	0	40	25
Irritability	0	0	46.7	50

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Solicited Injection Site or Systemic Reaction Within Seven Days Following the Second Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or Intramuscular Route

End point title	Percentage of Subjects Reporting Solicited Injection Site or Systemic Reaction Within Seven Days Following the Second Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or Intramuscular Route ^[3]
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End point description:

Solicited injection site reactions (children 3–8 years): Pain, Erythema, Edema, and Induration. Solicited systemic reactions (children 3–8 years): Fever, Headache, Malaise, and Myalgia. Solicited injection site reactions (infants 6–35 months): Tenderness, Erythema, Swelling, and Induration. Solicited systemic reactions (infants 6–35 months): Fever, Vomiting, Abnormal crying, Drowsiness, Appetite loss, and Irritability.

End point type	Primary
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End point timeframe:

Day 0 (pre-vaccination) up to 7 days post-second 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	ID Group (Age 3–8 years)	IM Group (Age 3–8 years)	ID Group (Age 6–35 months)	IM Group (Age 6–35 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain	53.3	45	0	0
Injection site Erythema	80	25	80	20
Injection site Edema	43.3	5	0	0
Injection site Induration	40	20	50	10
Fever	0	10	13.3	30
Headache	3.3	0	0	0
Malaise	6.7	5	0	0
Myalgia	0	5	0	0
Injection site Tenderness	0	0	43.3	10
Injection site Swelling	0	0	23.3	15
Vomiting	0	0	13.3	5
Abnormal crying	0	0	26.7	15
Drowsiness	0	0	23.3	5
Appetite loss	0	0	26.7	25

Irritability	0	0	40	45
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Statistical analyses

No statistical analyses for this end point

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

End point title	Geometric Mean Titers (GMTs) of influenza Vaccine Antibodies Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or Intramuscular Route
End point description:	Antibody titers were evaluated using the hemagglutination inhibition technique.
End point type	Secondary
End point timeframe:	Day 0 (pre-vaccination), Day 28 and Day 56 post-vaccination.

End point values	ID Group (Age 3–8 years)	IM Group (Age 3–8 years)	ID Group (Age 6–35 months)	IM Group (Age 6–35 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Titers				
geometric mean (confidence interval 95%)				
A/New Caledonia/20/99 (Day 0)	9.77 (6.11 to 15.63)	6.95 (4.32 to 11.18)	6.3 (4.54 to 8.75)	6.83 (4.21 to 11.09)
A/Wellington/1/2004 (Day 0)	80 (39 to 164.2)	113.1 (50.3 to 254.4)	6.91 (4.66 to 10.24)	10 (4.74 to 21.11)
B/Jiangsu/10/2003 (Day 0)	5.95 (4.99 to 7.09)	5.74 (4.74 to 6.96)	5 (5 to 5)	5 (5 to 5)
A/New Caledonia/20/99 (Day 28)	40.5 (20.2 to 81)	38.6 (19.6 to 75.7)	19.3 (10.2 to 36.3)	18.59 (9.56 to 36.15)
A/Wellington/1/2004 (Day 28)	775 (321 to 1869)	1428 (648 to 3145)	57.3 (33 to 99.3)	104.8 (44.7 to 245.5)
B/Jiangsu/10/2003 (Day 28)	15.69 (8.73 to 28.22)	16.97 (8.99 to 32.05)	6.73 (5.46 to 8.3)	7.07 (5.58 to 8.96)
A/New Caledonia/20/99 (Day 56)	134.5 (79.9 to 226.5)	169 (106 to 268)	87 (48.3 to 156.6)	115.1 (72.7 to 182.4)
A/Wellington/1/2004 (Day 56)	1594 (984 to 2583)	1328 (765 to 2303)	261 (150 to 455)	413 (240 to 710)
B/Jiangsu/10/2003 (Day 56)	50.4 (32.1 to 79.1)	58.6 (39.1 to 87.7)	26.3 (16.9 to 40.9)	23.8 (15.5 to 36.4)

Statistical analyses

Secondary: Geometric Mean Titer Ratios (GMTRs) of Influenza vaccine Antibodies After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or Intramuscular Route

End point title	Geometric Mean Titer Ratios (GMTRs) of Influenza vaccine Antibodies After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or Intramuscular Route
End point description:	Antibodies 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 three vaccine strains evaluated at Day 28/Day 0, Day 56/Day 0, and Day 56/Day 28.
End point type	Secondary
End point timeframe:	Day 0 (pre-vaccination) and Day 28 and Day 56 post-vaccination

End point values	ID Group (Age 3–8 years)	IM Group (Age 3–8 years)	ID Group (Age 6–35 months)	IM Group (Age 6–35 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Titer ratios				
geometric mean (confidence interval 95%)				
A/New Caledonia/20/99 (Day 28/Day 0)	4.14 (2.87 to 5.98)	5.45 (3.89 to 7.65)	3.01 (2.08 to 4.35)	2.68 (1.87 to 3.83)
A/Wellington/1/2004 (Day 28/Day 0)	10.41 (6.66 to 16.26)	10.71 (6.37 to 18.02)	8.1 (5.34 to 12.28)	10.08 (6.55 to 15.5)
B/Jiangsu/10/2003 (Day 28/Day 0)	2.64 (1.68 to 4.15)	2.93 (1.82 to 4.73)	1.35 (1.09 to 1.66)	1.41 (1.12 to 1.79)
A/New Caledonia/20/99 (Day 56/Day 0)	13.8 (10.3 to 18.5)	24.3 (16.3 to 36)	13.7 (8.58 to 21.88)	16.9 (10.5 to 27)
A/Wellington/1/2004 (Day 56/Day 0)	19.9 (13.1 to 30.4)	12.62 (7.08 to 22.52)	37.4 (21.6 to 64.6)	41.3 (26.1 to 65.3)
B/Jiangsu/10/2003 (Day 56/Day 0)	8.48 (5.91 to 12.15)	10.2 (7.22 to 14.4)	5.27 (3.39 to 8.18)	4.76 (3.11 to 7.28)
A/New Caledonia/20/99 (Day 56/Day 28)	3.32 (2.36 to 4.68)	4.46 (2.88 to 6.92)	4.32 (2.77 to 6.74)	5.76 (3.75 to 8.85)
A/Wellington/1/2004 (Day 56/Day 28)	1.95 (1.21 to 3.16)	1.039 (0.712 to 1.517)	4.55 (3.13 to 6.62)	3.86 (2.8 to 5.31)
B/Jiangsu/10/2003 (Day 56/Day 28)	3.21 (2.2 to 4.69)	3.46 (2.13 to 5.62)	3.66 (2.55 to 5.24)	3.04 (2.39 to 3.87)

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects Achieving Seroconversion or Significant Increase in Influenza Vaccine Antibodies Following Vaccination
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End point description:

Antibodies were evaluated using the hemagglutination inhibition technique. Seroconversion was defined as the following: for subjects with a pre-vaccination titer <10 (1/dil), post-injection titer ≥40 (1/dil) on Day 28 and Day 56 or significant increase and for subjects with a pre-vaccination titer ≥10 (1/dil), ≥ four-fold increase from pre- to post-injection titer on Day 28 and Day 56.

End point type	Secondary
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End point timeframe:

Day 0 (pre-vaccination), Day 28 and Day 56 post-vaccination

End point values	ID Group (Age 3–8 years)	IM Group (Age 3–8 years)	ID Group (Age 6–35 months)	IM Group (Age 6–35 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Percentage of subjects				
number (not applicable)				
A/New Caledonia/20/99 (Day 28/Day 0)	33.3	36.8	17.9	21.1
A/Wellington/1/2004 (Day 28/Day 0)	75.9	84.2	53.6	88.9
B/Jiangsu/10/2003 (Day 28/Day 0)	20	21.1	0	0
A/New Caledonia/20/99 (Day 56/Day 0)	83.3	95	72.4	85
A/Wellington/1/2004 (Day 56/Day 0)	96.7	89.5	89.7	100
B/Jiangsu/10/2003 (Day 56/Day 0)	56.7	75	37.9	35
A/New Caledonia/20/99 (Day 56/Day 28)	50	73.7	55.6	78.9
A/Wellington/1/2004 (Day 56/Day 28)	34.5	11.1	66.7	73.7
B/Jiangsu/10/2003 (Day 56/Day 28)	33.3	47.4	33.3	21.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Seroprotection Against Influenza Vaccine Antigens Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or Intramuscular Route

End point title	Percentage of Subjects with Seroprotection Against Influenza Vaccine Antigens Before and After Vaccination with Inactivated, Split-Virion Influenza Vaccine Administered by Either Intradermal or Intramuscular Route
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End point description:

Antibodies were evaluated using the hemagglutination inhibition technique. Seroprotection was defined as antibody titers of ≥40 [1/dil] on Day 28 and Day 56.

End point type	Secondary
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End point timeframe:

Day 0 (pre-vaccination), Day 28 and Day 56 post-vaccination

End point values	ID Group (Age 3–8 years)	IM Group (Age 3–8 years)	ID Group (Age 6-35 months)	IM Group (Age 6-35 months)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	30	20
Units: Percentage of subjects				
number (not applicable)				
A/New Caledonia/20/99 (Day 0)	23.3	10	6.7	5
A/Wellington/1/2004 (Day 0)	70	80	6.7	15.8
B/Jiangsu/10/2003 (Day 0)	0	0	0	0
A/New Caledonia/20/99 (Day 28)	40	36.8	17.9	21.1
A/Wellington/1/2004 (Day 28)	82.8	94.7	57.1	88.9
B/Jiangsu/10/2003 (Day 28)	20	21.1	0	0
A/New Caledonia/20/99 (Day 56)	86.7	95	72.4	95
A/Wellington/1/2004 (Day 56)	100	100	93.1	100
B/Jiangsu/10/2003 (Day 56)	56.7	75	37.9	35

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 (post-vaccination) up to Day 28 post-vaccination.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	7.1
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Reporting groups

Reporting group title	ID 9 µg (3–8 years)
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Reporting group description:

Subjects received 2 intradermal doses of the 9 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28 in children aged 3–8 years.

Reporting group title	IM 15 µg (3–8 years)
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Reporting group description:

Subjects received 2 intramuscular (IM) doses of the 15 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28 in children aged 3–8 years.

Reporting group title	ID 9 µg (6–35 months)
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Reporting group description:

Subjects received 2 intradermal (ID) doses of the 9 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28 in infants aged 6–35 months.

Reporting group title	IM 7.5 µg (6–35 months)
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Reporting group description:

Subjects received 2 intramuscular (IM) doses of the 7.5 µg formulation of inactivated, split-virion influenza vaccine administered on Day 0 and Day 28 in infants aged 6–35 months.

Serious adverse events	ID 9 µg (3–8 years)	IM 15 µg (3–8 years)	ID 9 µg (6–35 months)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 30 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Bronchiolitis			
alternative dictionary used: MedDRA 8.1			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 30 (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

Serious adverse events	IM 7.5 µg (6–35 months)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events	0		
Infections and infestations			
Bronchiolitis			
alternative dictionary used: MedDRA 8.1			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ID 9 µg (3–8 years)	IM 15 µg (3–8 years)	ID 9 µg (6–35 months)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 30 (90.00%)	13 / 20 (65.00%)	24 / 30 (80.00%)
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 30 (10.00%)	2 / 20 (10.00%)	0 / 30 (0.00%)
occurrences (all)	3	2	0
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	13 / 30 (43.33%)
occurrences (all)	0	0	13
General disorders and administration site conditions			
Injection site haemorrhage			
subjects affected / exposed	0 / 30 (0.00%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Pyrexia			
subjects affected / exposed	5 / 30 (16.67%)	2 / 20 (10.00%)	10 / 30 (33.33%)
occurrences (all)	5	2	10
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 30 (63.33%)	13 / 20 (65.00%)	0 / 30 (0.00%)
occurrences (all)	19	13	0
Injection site erythema			
alternative assessment type: Systematic			

subjects affected / exposed	27 / 30 (90.00%)	7 / 20 (35.00%)	24 / 30 (80.00%)
occurrences (all)	27	7	24
Injection site edema			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 30 (56.67%)	2 / 20 (10.00%)	0 / 30 (0.00%)
occurrences (all)	17	2	0
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 30 (46.67%)	6 / 20 (30.00%)	16 / 30 (53.33%)
occurrences (all)	14	6	16
Injection site tenderness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	13 / 30 (43.33%)
occurrences (all)	0	0	13
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 30 (3.33%)	4 / 20 (20.00%)	8 / 30 (26.67%)
occurrences (all)	1	4	8
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 30 (13.33%)	4 / 20 (20.00%)	0 / 30 (0.00%)
occurrences (all)	4	4	0
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	7 / 30 (23.33%)
occurrences (all)	0	0	7
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 30 (3.33%)	2 / 20 (10.00%)	1 / 30 (3.33%)
occurrences (all)	1	2	1
Eye disorders			
Conjunctivitis			
subjects affected / exposed	3 / 30 (10.00%)	1 / 20 (5.00%)	2 / 30 (6.67%)
occurrences (all)	3	1	2
Gastrointestinal disorders			

Abdominal pain subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	1 / 20 (5.00%) 1	0 / 30 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	2 / 30 (6.67%) 2
Stomatitis subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 30 (0.00%) 0
Teething subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	4 / 30 (13.33%) 4
Vomiting alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	4 / 30 (13.33%) 4
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 30 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	8 / 30 (26.67%) 8	6 / 20 (30.00%) 6	11 / 30 (36.67%) 11
Pharyngolaryngeal pain subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	0 / 20 (0.00%) 0	1 / 30 (3.33%) 1
Skin and subcutaneous tissue disorders Rash papular subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	1 / 20 (5.00%) 1	0 / 30 (0.00%) 0
Psychiatric disorders Restlessness subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 30 (0.00%) 0
Abnormal crying alternative assessment type: Systematic			

subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	16 / 30 (53.33%)
occurrences (all)	0	0	16
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	19 / 30 (63.33%)
occurrences (all)	0	0	19
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 30 (3.33%)	2 / 20 (10.00%)	0 / 30 (0.00%)
occurrences (all)	1	2	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 30 (3.33%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Eye infection			
subjects affected / exposed	0 / 30 (0.00%)	1 / 20 (5.00%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	3 / 30 (10.00%)	2 / 20 (10.00%)	0 / 30 (0.00%)
occurrences (all)	3	2	0
Nasopharyngitis			
subjects affected / exposed	4 / 30 (13.33%)	2 / 20 (10.00%)	1 / 30 (3.33%)
occurrences (all)	4	2	1
Otitis media			
subjects affected / exposed	5 / 30 (16.67%)	4 / 20 (20.00%)	10 / 30 (33.33%)
occurrences (all)	5	4	10
Rhinitis			
subjects affected / exposed	4 / 30 (13.33%)	5 / 20 (25.00%)	13 / 30 (43.33%)
occurrences (all)	4	5	13
Upper respiratory tract infection			
subjects affected / exposed	2 / 30 (6.67%)	1 / 20 (5.00%)	1 / 30 (3.33%)
occurrences (all)	2	1	1
Bronchiolitis			

subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 30 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 30 (0.00%) 0
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	2 / 30 (6.67%) 2
Appetite lost alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	15 / 30 (50.00%) 15

Non-serious adverse events	IM 7.5 µg (6-35 months)		
Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 20 (60.00%)		
Nervous system disorders Headache alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Drowsiness alternative assessment type: Systematic subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3		
General disorders and administration site conditions Injection site haemorrhage subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Pyrexia subjects affected / exposed occurrences (all)	5 / 20 (25.00%) 5		
Injection site pain alternative assessment type: Systematic			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	5		
Injection site edema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Injection site tenderness			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 20 (20.00%)		
occurrences (all)	4		
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 20 (50.00%)		
occurrences (all)	10		
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Eye disorders			

Conjunctivitis subjects affected / exposed occurrences (all)	5 / 20 (25.00%) 5		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all) Teething subjects affected / exposed occurrences (all) Vomiting alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 0 / 20 (0.00%) 0 1 / 20 (5.00%) 1 0 / 20 (0.00%) 0 1 / 20 (5.00%) 1		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Pharyngolaryngeal pain subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 4 / 20 (20.00%) 4 1 / 20 (5.00%) 1		
Skin and subcutaneous tissue disorders Rash papular subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Psychiatric disorders			

Restlessness subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3		
Abnormal crying alternative assessment type: Systematic subjects affected / exposed occurrences (all)	6 / 20 (30.00%) 6		
Irritability alternative assessment type: Systematic subjects affected / exposed occurrences (all)	12 / 20 (60.00%) 12		
Musculoskeletal and connective tissue disorders Myalgia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Eye infection subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Gastroenteritis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Otitis media subjects affected / exposed occurrences (all)	7 / 20 (35.00%) 7		
Rhinitis subjects affected / exposed occurrences (all)	12 / 20 (60.00%) 12		
Upper respiratory tract infection			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Bronchiolitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pneumonia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 20 (20.00%)</p> <p>4</p> <p>1 / 20 (5.00%)</p> <p>1</p> <p>1 / 20 (5.00%)</p> <p>1</p>		
<p>Metabolism and nutrition disorders</p> <p>Anorexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Appetite lost</p> <p>alternative assessment type: Systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 20 (0.00%)</p> <p>0</p> <p>7 / 20 (35.00%)</p> <p>7</p>		

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