



## Clinical trial results:

### A Phase 2, Open-Label, Single-Arm Trial to Evaluate the Shedding and Safety of CAIV-T Administered to Children 6 to <60 Months of Age

#### Summary

EudraCT number	2017-000848-17
Trial protocol	Outside EU/EEA
Global end of trial date	27 December 2006

#### Results information

Result version number	v1 (current)
This version publication date	03 January 2018
First version publication date	03 January 2018

#### Trial information

##### Trial identification

Sponsor protocol code	MI-CP129
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00344305
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States, MD 20878
Public contact	Raburn Mallory MD/ Sr Dir Clinical Development, MedImmune, LLC, +1 3013980000, clinicaltrialenquiries@medimmune.com
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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	27 December 2006
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 December 2006
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this study was to describe the percentage of participants who shed vaccine strain viruses.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 May 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	United States: 200
Worldwide total number of subjects	200
EEA total number of subjects	0

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)	92
Children (2-11 years)	108
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0
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## Subject disposition

### Recruitment

Recruitment details:

A total of 200 participants were enrolled in the study from 15-May-2006 through 22-Jun-2006 at 16 sites in the United States of America.

### Pre-assignment

Screening details:

A total of 200 participants were stratified on the basis of their age into two cohorts: Cohort 1 (participants aged between 6 to less than [ $<$ ] 24 months) and Cohort 2 (participants aged between 24 to  $<$  60 months).

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Cohort 1: Participants Between 6 to $<$ 24 Months Age

Arm description:

Participants received a single, intranasal dose of 0.2 millilitre (mL) (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained  $10^7$  fluorescent focus units (FFU) of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).

Arm type	Experimental
Investigational medicinal product name	FluMist
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, solution in single-dose container
Routes of administration	Intranasal use

Dosage and administration details:

Participants received a single, intranasal dose of 0.2 mL (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained  $10^7$  FFU of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).

<b>Arm title</b>	Cohort 2: Participants Between 24 to $<$ 60 Months Age
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Arm description:

Participants received a single, intranasal dose of 0.2 mL (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained  $10^7$  FFU of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).

Arm type	Experimental
Investigational medicinal product name	FluMist
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, solution in single-dose container
Routes of administration	Intranasal use

Dosage and administration details:

Participants received a single, intranasal dose of 0.2 mL (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained  $10^7$  FFU of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).

<b>Number of subjects in period 1</b>	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age
Started	100	100
Completed	98	99
Not completed	2	1
Participant was not contacted in window	-	1
Lost to follow-up	2	-

## Baseline characteristics

### Reporting groups

Reporting group title	Cohort 1: Participants Between 6 to < 24 Months Age
Reporting group description:	
Participants received a single, intranasal dose of 0.2 millilitre (mL) (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained 10 <sup>7</sup> fluorescent focus units (FFU) of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).	
Reporting group title	Cohort 2: Participants Between 24 to < 60 Months Age
Reporting group description:	
Participants received a single, intranasal dose of 0.2 mL (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained 10 <sup>7</sup> FFU of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).	

Reporting group values	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age	Total
Number of subjects	100	100	200
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	92	0	92
Children (2-11 years)	8	100	108
Age continuous Units: months			
arithmetic mean	14.87	41.31	
standard deviation	± 5.50	± 9.98	-
Gender categorical Units: Subjects			
Female	51	53	104
Male	49	47	96
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	7	15	22
Not Hispanic or Latino	93	85	178
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	0	2	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	14	7	21
White	86	89	175
More than one race	0	1	1
Unknown or Not Reported	0	0	0
History of laboratory-confirmed influenza illness Units: Subjects			

Positive	1	2	3
Negative	99	98	197
History of receiving an influenza vaccine			
Units: Subjects			
Positive	43	73	116
Negative	57	27	84

## Subject analysis sets

Subject analysis set title	All Participants
Subject analysis set type	Full analysis

Subject analysis set description:

Participants between 6 to < 60 months age received a single, intranasal dose of 0.2 mL (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained 10<sup>7</sup> FFU of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).

Reporting group values	All Participants		
Number of subjects	200		
Age categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)	92		
Children (2-11 years)	108		
Age continuous			
Units: months			
arithmetic mean	28.09		
standard deviation	± 15.50		
Gender categorical			
Units: Subjects			
Female	104		
Male	96		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	22		
Not Hispanic or Latino	178		
Unknown or Not Reported	0		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1		
Asian	2		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	21		
White	175		
More than one race	1		
Unknown or Not Reported	0		
History of laboratory-confirmed influenza illness			
Units: Subjects			
Positive	3		
Negative	197		

History of receiving an influenza vaccine			
Units: Subjects			
Positive	116		
Negative	84		



## End points

### End points reporting groups

Reporting group title	Cohort 1: Participants Between 6 to < 24 Months Age
Reporting group description: Participants received a single, intranasal dose of 0.2 millilitre (mL) (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained 10 <sup>7</sup> fluorescent focus units (FFU) of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).	
Reporting group title	Cohort 2: Participants Between 24 to < 60 Months Age
Reporting group description: Participants received a single, intranasal dose of 0.2 mL (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained 10 <sup>7</sup> FFU of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).	
Subject analysis set title	All Participants
Subject analysis set type	Full analysis
Subject analysis set description: Participants between 6 to < 60 months age received a single, intranasal dose of 0.2 mL (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained 10 <sup>7</sup> FFU of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).	

### Primary: Percentage of Participants Who Shed Any Vaccine Virus

End point title	Percentage of Participants Who Shed Any Vaccine Virus <sup>[1]</sup>
End point description: Viral shedding is defined as the detection of virus by viral culture and vaccine-type virus was confirmed by polymerase chain reaction (PCR) based assays. Viral shedding (A/New Caledonia/20/99 [H1N1]; A/Wyoming/03/2003 [H3N2] (A/Fujian/411/2002-like); B/Jilin/20/2003 [B/Shanghai/361/2002-like]) was measured from samples obtained from nasal swabs daily from Days 1 to 7 post vaccination and approximately every other day thereafter from Days 9 to 28. Participants whose Day 25 or 28 shedding sample was positive for vaccine virus had additional shedding samples collected approximately every 7 days, or as soon as possible upon awareness of culture positivity, until 2 consecutive samples were negative for vaccine virus. Shedding population included all participants who received a full dose of study drug and had assay results from nasal specimens obtained at any post-dosing time point. Here, number of participants analyzed signified those participants who were evaluable for this endpoint.	
End point type	Primary
End point timeframe: Days 1-28 after study vaccination (up to Day 28)	

#### 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: Statistical analysis was not applicable since there were no inferential statistics planned for primary outcome measures, only descriptive statistics were reported.

End point values	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	100		
Units: percentage of participants				
number (confidence interval 95%)	88.9 (81.0 to 94.3)	69.0 (59.0 to 77.9)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Participants Who Shed A/H1N1 Vaccine Virus

End point title	Percentage of Participants Who Shed A/H1N1 Vaccine Virus <sup>[2]</sup>
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End point description:

Viral shedding is defined as the detection of virus by viral culture and vaccine-type virus was confirmed by polymerase chain reaction (PCR) based assays. Viral shedding (A/New Caledonia/20/99 [H1N1]; A/Wyoming/03/2003 [H3N2] (A/Fujian/411/2002-like); B/Jilin/20/2003 B/Shanghai/361/2002-like)) was measured from samples obtained from nasal swabs daily from Days 1 to 7 post vaccination and approximately every other day thereafter from Days 9 to 28. Participants whose Day 25 or 28 shedding sample was positive for vaccine virus had additional shedding samples collected approximately every 7 days, or as soon as possible upon awareness of culture positivity, until 2 consecutive samples were negative for vaccine virus. Shedding population included all participants who received a full dose of study drug and had assay results from nasal specimens obtained at any post-dosing time point. Here, number of participants analyzed signified those participants who were evaluable for this endpoint.

End point type	Primary
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End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

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: Statistical analysis was not applicable since there were no inferential statistics planned for primary outcome measures, only descriptive statistics were reported.

End point values	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	100		
Units: percentage of participants				
number (confidence interval 95%)	76.8 (67.2 to 84.7)	52.0 (41.8 to 62.1)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Participants Who Shed A/H3N2 Vaccine Virus

End point title	Percentage of Participants Who Shed A/H3N2 Vaccine Virus <sup>[3]</sup>
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End point description:

Viral shedding is defined as the detection of virus by viral culture and vaccine-type virus was confirmed by polymerase chain reaction (PCR) based assays. Viral shedding (A/New Caledonia/20/99 [H1N1]; A/Wyoming/03/2003 [H3N2] (A/Fujian/411/2002-like); B/Jilin/20/2003 [B/Shanghai/361/2002-like]) was measured from samples obtained from nasal swabs daily from Days 1 to 7 post vaccination and

approximately every other day thereafter from Days 9 to 28. Participants whose Day 25 or 28 shedding sample was positive for vaccine virus had additional shedding samples collected approximately every 7 days, or as soon as possible upon awareness of culture positivity, until 2 consecutive samples were negative for vaccine virus. Shedding population included all participants who received a full dose of study drug and had assay results from nasal specimens obtained at any post-dosing time point. Here, number of participants analyzed signified those participants who were evaluable for this endpoint.

End point type	Primary
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End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

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: Statistical analysis was not applicable since there were no inferential statistics planned for primary outcome measures, only descriptive statistics were reported.

End point values	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	100		
Units: percentage of participants				
number (confidence interval 95%)	57.6 (47.2 to 67.5)	15.0 (8.6 to 23.5)		

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants Who Shed B Vaccine Virus

End point title	Percentage of Participants Who Shed B Vaccine Virus <sup>[4]</sup>
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End point description:

Viral shedding is defined as the detection of virus by viral culture and vaccine-type virus was confirmed by polymerase chain reaction (PCR) based assays. Viral shedding (A/New Caledonia/20/99 [H1N1]; A/Wyoming/03/2003 [H3N2] (A/Fujian/411/2002-like); B/Jilin/20/2003 [B/Shanghai/361/2002-like]) was measured from samples obtained from nasal swabs daily from Days 1 to 7 post vaccination and approximately every other day thereafter from Days 9 to 28. Participants whose Day 25 or 28 shedding sample was positive for vaccine virus had additional shedding samples collected approximately every 7 days, or as soon as possible upon awareness of culture positivity, until 2 consecutive samples were negative for vaccine virus. Shedding population included all participants who received a full dose of study drug and had assay results from nasal specimens obtained at any post-dosing time point. Here, number of participants analyzed signified those participants who were evaluable for this endpoint.

End point type	Primary
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End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

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: Statistical analysis was not applicable since there were no inferential statistics planned for primary outcome measures, only descriptive statistics were reported.

End point values	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	100		
Units: percentage of participants				
number (confidence interval 95%)	37.4 (27.9 to 47.7)	37.0 (27.6 to 47.2)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Any Vaccine Virus Shedding

End point title	Duration of Any Vaccine Virus Shedding
End point description: The number of days of shedding was summarized for all participants who shed any vaccine virus. Shedding population included all participants who received a full dose of study drug and had assay results from nasal specimens obtained at any post-dosing time point. Here, number of participants analyzed signified those participants who shed any confirmed strain virus.	
End point type	Secondary
End point timeframe: Days 1-28 after study vaccination (up to Day 28)	

End point values	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	69		
Units: days				
arithmetic mean (standard deviation)	3.0 (± 1.5)	2.7 (± 1.6)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Confirmed A/H1N1 Vaccine Virus Shedding

End point title	Duration of Confirmed A/H1N1 Vaccine Virus Shedding
End point description: The number of days of shedding was summarized for all participants who shed confirmed A/H1N1 strain virus. Shedding population included all participants who received a full dose of study drug and had assay results from nasal specimens obtained at any post-dosing time point. Here, number of participants analyzed signified those participants who shed any confirmed strain virus.	
End point type	Secondary

End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

End point values	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	52		
Units: days				
arithmetic mean (standard deviation)	2.1 ( $\pm$ 1.0)	2.2 ( $\pm$ 1.3)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Confirmed A/H3N2 Vaccine Virus Shedding

End point title	Duration of Confirmed A/H3N2 Vaccine Virus Shedding
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End point description:

The number of days of shedding was summarized for all participants who shed confirmed A/H3N2 strain virus. Shedding population included all participants who received a full dose of study drug and had assay results from nasal specimens obtained at any post-dosing time point. Here, number of participants analyzed signified those participants who shed any confirmed strain virus.

End point type	Secondary
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End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

End point values	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	15		
Units: days				
arithmetic mean (standard deviation)	1.8 ( $\pm$ 0.9)	1.7 ( $\pm$ 0.8)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Confirmed B Vaccine Virus Shedding

End point title	Duration of Confirmed B Vaccine Virus Shedding
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End point description:

The number of days of shedding was summarized for all participants who shed confirmed B strain virus. Shedding population included all participants who received a full dose of study drug and had assay results from nasal specimens obtained at any post-dosing time point. Here, number of participants analyzed signified those participants who shed any confirmed strain virus.

End point type	Secondary
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End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

End point values	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	37		
Units: days				
arithmetic mean (standard deviation)	2.1 (± 1.5)	1.8 (± 1.2)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Quantitation of Confirmed A/H1N1 Shed Vaccine Virus on Any Day

End point title	Quantitation of Confirmed A/H1N1 Shed Vaccine Virus on Any Day
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End point description:

Quantitation of confirmed A/H1N1 shed vaccine virus was evaluated using the log transformed median tissue culture infectious dose (TCID<sub>50</sub>) per (/) millilitre (mL) for A/H1N1 vaccine strain and summarized for all participants who shed vaccine virus. Shedding population included all participants who received a full dose of study drug and had assay results from nasal specimens obtained at any post-dosing time point. Here, number of participants analyzed signified those participants who shed any confirmed strain virus.

End point type	Secondary
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End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

End point values	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	45		
Units: log (TCID <sub>50</sub> )/mL				
arithmetic mean (standard deviation)	2.14 (± 0.98)	2.62 (± 0.97)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Quantitation of Confirmed A/H3N2 Shed Vaccine Virus on Any Day

End point title	Quantitation of Confirmed A/H3N2 Shed Vaccine Virus on Any Day
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End point description:

Quantitation of confirmed A/H3N2 shed vaccine virus was evaluated using the log (TCID<sub>50</sub>)/mL for A/H3N2 vaccine strain and summarized for all participants who shed vaccine virus. Shedding population included all participants who received a full dose of study drug and had assay results from nasal specimens obtained at any post-dosing time point. Here, number of participants analyzed signified those participants who shed any confirmed strain virus.

End point type	Secondary
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End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

End point values	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	5		
Units: log (TCID <sub>50</sub> )/mL				
arithmetic mean (standard deviation)	1.59 (± 0.95)	1.10 (± 0.53)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Quantitation of Confirmed B Shed Vaccine Virus on Any Day

End point title	Quantitation of Confirmed B Shed Vaccine Virus on Any Day
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End point description:

Quantitation of confirmed B shed vaccine virus was evaluated using the log (TCID<sub>50</sub>)/mL for B vaccine strain and summarized for all participants who shed vaccine virus. Shedding population included all participants who received a full dose of study drug and had assay results from nasal specimens obtained at any post-dosing time point. Here, number of participants analyzed signified those participants who shed any confirmed strain virus.

End point type	Secondary
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End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

<b>End point values</b>	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	29		
Units: log (TCID50)/mL				
arithmetic mean (standard deviation)	1.70 (± 1.09)	1.24 (± 0.68)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Genotypic and Phenotypic Stability of A/H1N1 Shed Vaccine Virus

End point title	Number of Participants With Genotypic and Phenotypic Stability of A/H1N1 Shed Vaccine Virus
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End point description:

The genetic and phenotypic stability of shed vaccine virus was evaluated by determination of genomic sequence and assessment of the cold-adapted (ca) and temperature-sensitive (ts) phenotypes. Viruses were considered ts if their titer at 39 degrees Celsius (°C) was at least two logs (100-fold) lower than their titer at 33°C. Viruses were considered ca if they replicated at 25°C to a titer that was no more than two logs (100-fold) lower than the titer at 33°C. After additional phenotypic and genotypic analyses, all evaluable samples retained the ca and ts phenotypes. Here, number of participants analyzed signified those participants who were evaluable for this endpoint and "n" signified those participants who were evaluable for a specified category. The number 99999 signified data not available because no participant was evaluable for the specified category.

End point type	Secondary
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End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

<b>End point values</b>	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	93			
Units: participants				
Genotypic Stability (n=0)	99999			
Phenotypic Stability (n=93)	90			

### Statistical analyses

No statistical analyses for this end point



## Secondary: Number of Participants With Genotypic and Phenotypic Stability of A/H3N2 Shed Vaccine Virus

End point title	Number of Participants With Genotypic and Phenotypic Stability of A/H3N2 Shed Vaccine Virus
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End point description:

The genetic and phenotypic stability of shed vaccine virus was evaluated by determination of genomic sequence and assessment of the ca and ts phenotypes. Viruses were considered ts if their titer at 39°C was at least two logs (100-fold) lower than their titer at 33°C. Viruses were considered ca if they replicated at 25°C to a titer that was no more than two logs (100-fold) lower than the titer at 33°C. After additional phenotypic and genotypic analyses, all evaluable samples retained the ca and ts phenotypes. Here, number of participants analyzed signified those participants who were evaluable for this endpoint and "n" signified those participants who were evaluable for a specified category. The number 99999 signified data not available because no participant was evaluable for the specified category.

End point type	Secondary
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End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

<b>End point values</b>	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	39			
Units: participants				
Genotypic Stability (n=0)	99999			
Phenotypic Stability (n=39)	37			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Genotypic and Phenotypic Stability of B Shed Vaccine Virus

End point title	Number of Participants With Genotypic and Phenotypic Stability of B Shed Vaccine Virus
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End point description:

The genetic and phenotypic stability of shed vaccine virus was evaluated by determination of genomic sequence and assessment of the ca and ts phenotypes. Viruses were considered ts if their titer at 37°C was at least two logs (100-fold) lower than their titer at 33°C. Viruses were considered ca if they replicated at 25°C to a titer that was no more than two logs (100-fold) lower than the titer at 33°C. After additional phenotypic and genotypic analyses, all evaluable samples retained the ca and ts phenotypes. Here, number of participants analyzed signified those participants who were evaluable for this endpoint and "n" signified those participants who were evaluable for a specified category.

End point type	Secondary
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End point timeframe:

Days 1-28 after study vaccination (up to Day 28)

<b>End point values</b>	All Participants			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: participants				
Genotypic Stability (n=33)	33			
Phenotypic Stability (n=61)	29			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Reactogenicity Events (REs) and Adverse Events (AEs) Through 28 Days Post Vaccination

End point title	Number of Participants With Reactogenicity Events (REs) and Adverse Events (AEs) Through 28 Days Post Vaccination
End point description: REs were predefined solicited events that could potentially occur after vaccination. The REs for this study were fever, runny/stuffy nose, sore throat, cough, vomiting, headache, abdominal pain (stomach ache), muscle ache, chills, decreased activity level (lethargy), decreased appetite, and irritability. An AE was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Safety population included all participants who received any study drug and had experienced any follow-up for safety.	
End point type	Secondary
End point timeframe: Days 0-28 after vaccination (up to Day 28)	

<b>End point values</b>	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	100		
Units: participants				
Any REs	84	77		
AEs	48	31		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Serious Adverse Events (SAEs) and Significant New Medical Conditions (SNMC) Through 180 Days Post Vaccination

End point title	Number of Participants With Serious Adverse Events (SAEs) and Significant New Medical Conditions (SNMC) Through 180 Days Post Vaccination			
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**End point description:**

An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. An SNMC is defined as a newly diagnosed medical condition that was of a chronic, ongoing nature and was assessed by the investigator as medically significant. SNMCs included, but were not limited to, diabetes, asthma, autoimmune disease (lupus, rheumatoid arthritis), and neurological disease (epilepsy, autism). Safety population included all participants who received any study drug and had experienced any follow-up for safety.

End point type	Secondary
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**End point timeframe:**

Days 0-180 after vaccination (up to 6.5 months)

<b>End point values</b>	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	100		
Units: participants				
SAEs	1	0		
SNMC	1	1		

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of Participants With REs in Relation to Any Vaccine Virus Shedding**

End point title	Number of Participants With REs in Relation to Any Vaccine Virus Shedding
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**End point description:**

REs were predefined solicited events that could potentially occur after vaccination. The REs for this study were fever, runny/stuffy nose, sore throat, cough, vomiting, headache, abdominal pain (stomach ache), muscle ache, chills, decreased activity level (lethargy), decreased appetite, and irritability. Safety population included all participants who received any study drug and had experienced any follow-up for safety. Here, number of participants analyzed signified those participants who had REs.

End point type	Secondary
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**End point timeframe:**

Days 0-28 after study vaccination (up to Day 28)

<b>End point values</b>	Cohort 1: Participants Between 6 to < 24 Months Age	Cohort 2: Participants Between 24 to < 60 Months Age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	77		
Units: participants	75	55		

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs - Days 0-28 post dosing (up to Day 28); SAEs - Days 0-180 post dosing (up to 6.5 months).

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.0
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### Reporting groups

Reporting group title	Cohort 2: Participants Between 24 to < 60 Months Age
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Reporting group description:

Participants received a single, intranasal dose of 0.2 mL (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained 10<sup>7</sup> FFU of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).

Reporting group title	Cohort1: Participants Between 6 to < 24 Months Age
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Reporting group description:

Participants received a single, intranasal dose of 0.2 mL (approximately 0.1 mL in each nostril) FluMist trivalent influenza virus vaccine live on Day 0 of the study. Each dose of FluMist vaccine contained 10<sup>7</sup> FFU of three influenza virus strains namely, A/New Caledonia/20/99 (H1N1), A/Wyoming/03/2003 (H3N2) (A/Fujian/411/2002-like) and B/Jilin/20/2003 (B/Shanghai/361/2002-like).

Serious adverse events	Cohort 2: Participants Between 24 to < 60 Months Age	Cohort1: Participants Between 6 to < 24 Months Age	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Cohort 2: Participants Between 24 to < 60 Months Age	Cohort1: Participants Between 6 to < 24 Months Age	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 100 (25.00%)	48 / 100 (48.00%)	

Investigations BODY TEMPERATURE INCREASED subjects affected / exposed occurrences (all)	2 / 100 (2.00%) 2	3 / 100 (3.00%) 4	
Injury, poisoning and procedural complications ARTHROPOD BITE subjects affected / exposed occurrences (all)  ARTHROPOD STING subjects affected / exposed occurrences (all)	3 / 100 (3.00%) 3  2 / 100 (2.00%) 2	4 / 100 (4.00%) 4  0 / 100 (0.00%) 0	
Ear and labyrinth disorders OTORRHOEA subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	2 / 100 (2.00%) 2	
Eye disorders CONJUNCTIVITIS subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	2 / 100 (2.00%) 2	
Gastrointestinal disorders DIARRHOEA subjects affected / exposed occurrences (all)  FLATULENCE subjects affected / exposed occurrences (all)  TEETHING subjects affected / exposed occurrences (all)	9 / 100 (9.00%) 11  0 / 100 (0.00%) 0  0 / 100 (0.00%) 0	5 / 100 (5.00%) 6  2 / 100 (2.00%) 4  21 / 100 (21.00%) 30	
Respiratory, thoracic and mediastinal disorders EPISTAXIS subjects affected / exposed occurrences (all)	2 / 100 (2.00%) 2	3 / 100 (3.00%) 3	
Skin and subcutaneous tissue disorders ECZEMA subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	2 / 100 (2.00%) 2	

HEAT RASH subjects affected / exposed occurrences (all)	2 / 100 (2.00%) 2	0 / 100 (0.00%) 0	
Infections and infestations HERPANGINA subjects affected / exposed occurrences (all)  OTITIS MEDIA subjects affected / exposed occurrences (all)  PHARYNGITIS STREPTOCOCCAL subjects affected / exposed occurrences (all)  VIRAL INFECTION subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0  0 / 100 (0.00%) 0  3 / 100 (3.00%) 3  2 / 100 (2.00%) 2	2 / 100 (2.00%) 2  4 / 100 (4.00%) 4  1 / 100 (1.00%) 1  3 / 100 (3.00%) 4	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 March 2006	The protocol was amended to add definition of Reactogenicity Events (REs).

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported