



## Clinical trial results:

### Immunogenicity and Tolerability Study of FLUVAL AB Novo Suspension for Injection (trivalent, seasonal influenza vaccine, active ingredient content: 6 g HA/strain/0.5 ml) for Children and Adolescents

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2013-003449-40   |
| Trial protocol           | HU               |
| Global end of trial date | 09 December 2014 |

#### Results information

|                                   |                                                             |
|-----------------------------------|-------------------------------------------------------------|
| Result version number             | v1                                                          |
| This version publication date     | 06 January 2017                                             |
| First version publication date    | 06 January 2017                                             |
| Summary attachment (see zip file) | 2013-003449-40-FSR-Synopsis (FABNovo-H-16-FSR_synopsis.pdf) |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | FABNovo-H-16 |
|-----------------------|--------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |                                                                                      |
|------------------------------|--------------------------------------------------------------------------------------|
| Sponsor organisation name    | Omninvest Ltd.                                                                       |
| Sponsor organisation address | Fő utca 7., Pilisborosjenő, Hungary, H-2097                                          |
| Public contact               | Clinical expert, Fluart Innovative Vaccines Ltd., 36 204197063, jeno.makra@fluart.hu |
| Scientific contact           | Study director, Omninvest Ltd., 36 204197136, brigitta.kozma@omninvest.hu            |

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:

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**Results analysis stage**

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|                                                      |                  |
|------------------------------------------------------|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 25 February 2015 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 09 December 2014 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 09 December 2014 |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

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Main objective of the trial:

Assessment immunogenicity and safety of Fluval AB Novo seasonal influenza vaccine with 3 x 6 µgHA active ingredient in two age groups (children and adolescents).

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 was also available on site in case of any immediate allergic reactions.

Background therapy:

-

Evidence for comparator:

-

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment                          | 18 October 2013 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | Yes             |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Hungary: 120 |
| Worldwide total number of subjects   | 120          |
| EEA total number of subjects         | 120          |

Notes:

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**Subjects enrolled per age group**

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|                                           |    |
|-------------------------------------------|----|
| 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)                     | 60 |
| Adolescents (12-17 years)                 | 60 |
| Adults (18-64 years)                      | 0  |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details:

healthy volunteers of full contractual capacity were planned to be enrolled in two age groups (3 to 11 years and 12 to 18 years) from both sexes

### Pre-assignment

Screening details:

Performance of brief physical examination, including measurement of heart rate, axillary temperature, blood pressure, check of the heart, lungs, and axillary lymph nodes, etc.

### Period 1

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

### Arms

| Arm title | Treatment |
|-----------|-----------|
|-----------|-----------|

Arm description:

Children 3-11 years:

Sixty (60) healthy volunteers of full contractual capacity from both sexes were enrolled.

Treatment: 0.5 x 6 µgHA/strain/0.5ml of Fluval AB Novo trivalent influenza vaccine was administered once at Day 0.

Adolescents 12-18 years:

Sixty (60) healthy volunteers of full contractual capacity from both sexes were enrolled.

Treatment: 1 x 6 µgHA/strain/0.5ml of Fluval AB Novo trivalent influenza vaccine was administered once at Day 0.

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Intervention           |
| Investigational medicinal product name | Fluval AB Novo         |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

Children 3-11 years:

Treatment: 0.5 x 6 µgHA/strain/0.5ml of Fluval AB Novo trivalent influenza vaccine was administered once at Day 0.

Adolescents 12-18 years:

Treatment: 1 x 6 µgHA/strain/0.5ml of Fluval AB Novo trivalent influenza vaccine was administered once at Day 0.

| Number of subjects in period 1 | Treatment |
|--------------------------------|-----------|
| Started                        | 120       |
| Completed                      | 120       |



## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Overall trial |
|-----------------------|---------------|

Reporting group description:

All one hundred and twenty (120) subjects entered in the study and were vaccinated (ITT population).

All one hundred and twenty (120) subjects attended visit at Day 21-28, all of whom (one hundred and twenty (120) subjects) data were available and evaluated (PP population).

| Reporting group values                                                                                                                                                                 | Overall trial | Total |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|-------|--|
| Number of subjects                                                                                                                                                                     | 120           | 120   |  |
| Age categorical                                                                                                                                                                        |               |       |  |
| Children 3-11 years: A child is belonging to age group 3-11 years, if he/she has already been turning 3 but has not yet been turning 12 on the day of vaccination.                     |               |       |  |
| Adolescents 12-18 years: An adolescent subject is belonging to age group 12-18 years, if he/she has already been turning 12 but has not yet been turning 18 on the day of vaccination. |               |       |  |
| Units: Subjects                                                                                                                                                                        |               |       |  |
| In utero                                                                                                                                                                               | 0             | 0     |  |
| Preterm newborn infants<br>(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)                                                                                                                                                              | 60            | 60    |  |
| Adults (18-64 years)                                                                                                                                                                   | 0             | 0     |  |
| From 65-84 years                                                                                                                                                                       | 0             | 0     |  |
| 85 years and over                                                                                                                                                                      | 0             | 0     |  |
| Children 3-11 years                                                                                                                                                                    | 60            | 60    |  |
| Age continuous                                                                                                                                                                         |               |       |  |
| Units: years                                                                                                                                                                           |               |       |  |
| median                                                                                                                                                                                 | 11            |       |  |
| full range (min-max)                                                                                                                                                                   | 3 to 17       | -     |  |
| Gender categorical                                                                                                                                                                     |               |       |  |
| Units: Subjects                                                                                                                                                                        |               |       |  |
| Female                                                                                                                                                                                 | 53            | 53    |  |
| Male                                                                                                                                                                                   | 67            | 67    |  |

## End points

### End points reporting groups

| Reporting group title                                                                                                                                                                                                                     | Treatment |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| Reporting group description:                                                                                                                                                                                                              |           |
| Children 3-11 years:<br>Sixty (60) healthy volunteers of full contractual capacity from both sexes were enrolled.<br>Treatment: 0.5 x 6 µgHA/strain/0.5ml of Fluval AB Novo trivalent influenza vaccine was administered once at Day 0.   |           |
| Adolescents 12-18 years:<br>Sixty (60) healthy volunteers of full contractual capacity from both sexes were enrolled.<br>Treatment: 1 x 6 µgHA/strain/0.5ml of Fluval AB Novo trivalent influenza vaccine was administered once at Day 0. |           |

### Primary: Geometric Mean Titers (GMTs) of influenza Antibodies Before and After Vaccination in subjects aged 3-11 years

| End point title                                                                                                                                                      | Geometric Mean Titers (GMTs) of influenza Antibodies Before and After Vaccination in subjects aged 3-11 years <sup>[1]</sup> |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|
| End point description:<br>Anti-hemagglutinin antibody titers were measured for each strain with the seroneutralization method. The GMTs were determined by HI titer. |                                                                                                                              |
| End point type                                                                                                                                                       | Primary                                                                                                                      |
| End point timeframe:<br>Day 0 (pre-vaccination) and Day 21-28 (post-vaccination)                                                                                     |                                                                                                                              |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive analysis was performed based on the study group and the study vaccine administered for this outcome.

| End point values                         | Treatment              |  |  |  |
|------------------------------------------|------------------------|--|--|--|
| Subject group type                       | Reporting group        |  |  |  |
| Number of subjects analysed              | 60 <sup>[2]</sup>      |  |  |  |
| Units: Titers (1/dil)                    |                        |  |  |  |
| geometric mean (confidence interval 95%) |                        |  |  |  |
| A/H1N1; Day 0                            | 31.8 (23.69 to 41.58)  |  |  |  |
| A/H1N1; Day 21                           | 136.1 (106 to 174.8)   |  |  |  |
| A/H3N2; Day 0                            | 92.96 (65.88 to 131.2) |  |  |  |
| A/H3N2; Day 21                           | 463.1 (349.8 to 613.2) |  |  |  |
| B/; Day 0                                | 17.82 (12.5 to 25.39)  |  |  |  |
| B/; Day 21                               | 75.95 (51.64 to 111.7) |  |  |  |

Notes:

[2] - PP population in Children aged 3-11 years: sixty (60) persons.

### Statistical analyses

No statistical analyses for this end point

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**Primary: Percentage of Subjects Aged 3-11 years With Seroconversion Against Influenza Antigens Before and After Vaccination**

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|                 |                                                                                                                                   |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects Aged 3-11 years With Seroconversion Against Influenza Antigens Before and After Vaccination <sup>[3]</sup> |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-hemagglutinin antibody titers were measured for each strain with the seroneutralization method. Seroconversion was defined as the proportion of subjects with a pre-vaccination titer < 10 (1/dil) to a post-vaccination titer ≥ 40 (1/dil). Significant increase was defined as proportion of subjects with a pre-vaccination titer ≥ 10 (1/dil) and ≥ 4-fold increase of the titer.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 21 post-vaccination/Day 0 (pre-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 analysis was performed based on the study group and the study vaccine administered for this outcome.

| End point values              | Treatment         |  |  |  |
|-------------------------------|-------------------|--|--|--|
| Subject group type            | Reporting group   |  |  |  |
| Number of subjects analysed   | 60 <sup>[4]</sup> |  |  |  |
| Units: Percentage of subjects |                   |  |  |  |
| number (not applicable)       |                   |  |  |  |
| A/H1N1; Day 21                | 61.67             |  |  |  |
| A/H3N2; Day 21                | 58.33             |  |  |  |
| B/; Day 21                    | 66.67             |  |  |  |

Notes:

[4] - PP population in Children aged 3-11 years: sixty (60) persons.

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**Statistical analyses**

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No statistical analyses for this end point

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**Primary: Geometric Mean Titers (GMTs) of Influenza Antibodies Before and After Vaccination with Fluval AB Novo in subjects 12-17 years.**

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|                 |                                                                                                                                               |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Geometric Mean Titers (GMTs) of Influenza Antibodies Before and After Vaccination with Fluval AB Novo in subjects 12-17 years. <sup>[5]</sup> |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-hemagglutinin antibody titers were measured for each strain with the seroneutralization method. The GMTs were determined by HI titer.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive analysis was performed based on the study group and the study vaccine administered for this outcome.

| End point values                         | Treatment              |  |  |  |
|------------------------------------------|------------------------|--|--|--|
| Subject group type                       | Reporting group        |  |  |  |
| Number of subjects analysed              | 60 <sup>[6]</sup>      |  |  |  |
| Units: 1/dil                             |                        |  |  |  |
| geometric mean (confidence interval 95%) |                        |  |  |  |
| A/H1N1; Day 0                            | 35.64 (26.06 to 48.74) |  |  |  |
| A/H1N1; Day 21                           | 167.6 (134 to 209.5)   |  |  |  |
| A/H3N2; Day 0                            | 69.64 (46.4 to 104.5)  |  |  |  |
| A/H3N2; Day 21                           | 417.4 (317.3 to 549)   |  |  |  |
| B/; Day 0                                | 20.47 (15.24 to 27.49) |  |  |  |
| B/; Day 21                               | 97.36 (75.4 to 125.7)  |  |  |  |

Notes:

[6] - PP population in Children aged 12-17 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects Aged 12 - 17 years With Seroconversion Against Influenza Antigens Before and After Vaccination

|                 |                                                                                                                                      |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects Aged 12 - 17 years With Seroconversion Against Influenza Antigens Before and After Vaccination <sup>[7]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-hemagglutinin antibody titers were measured for each strain with the seroneutralization method. Seroconversion was defined as the proportion of subjects with a pre-vaccination titer < 10 (1/dil) to a post-vaccination titer ≥ 40 (1/dil). Significant increase was defined as proportion of subjects with a pre-vaccination titer ≥ 10 (1/dil) and ≥ 4-fold increase of the titer. Anti-hemagglutinin antibody titers were measured for each strain with the seroneutralization method. Seroprotection was defined as antibody titers ≥ 40 (1/dil).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive analysis was performed based on the study group and the study vaccine administered for this outcome.

| End point values              | Treatment         |  |  |  |
|-------------------------------|-------------------|--|--|--|
| Subject group type            | Reporting group   |  |  |  |
| Number of subjects analysed   | 60 <sup>[8]</sup> |  |  |  |
| Units: Percentage of subjects |                   |  |  |  |
| number (not applicable)       |                   |  |  |  |
| A/H1N1; Day 21                | 66.67             |  |  |  |
| A/H3N2; Day 21                | 61.67             |  |  |  |
| B/; Day 21                    | 70                |  |  |  |

Notes:

[8] - PP population in Children aged 12-17 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

### Primary: Geometric Mean Titer Ratios (GMTRs) of influenza Antibodies After Vaccination in subjects aged 3-11 years

|                 |                                                                                                                          |
|-----------------|--------------------------------------------------------------------------------------------------------------------------|
| End point title | Geometric Mean Titer Ratios (GMTRs) of influenza Antibodies After Vaccination in subjects aged 3-11 years <sup>[9]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-hemagglutinin antibody titers were measured for each strain with the seroneutralization method. The GMTs were determined by HI titer.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

[9] - 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 analysis was performed based on the study group and the study vaccine administered for this outcome.

| End point values                         | Treatment              |  |  |  |
|------------------------------------------|------------------------|--|--|--|
| Subject group type                       | Reporting group        |  |  |  |
| Number of subjects analysed              | 60 <sup>[10]</sup>     |  |  |  |
| Units: Titer ratios (1/dil)              |                        |  |  |  |
| geometric mean (confidence interval 95%) |                        |  |  |  |
| A/H1N1                                   | 4.337 (3.432 to 5.48)  |  |  |  |
| A/H3N2                                   | 4.982 (3.847 to 6.451) |  |  |  |
| B/                                       | 4.262 (3.383 to 5.37)  |  |  |  |

Notes:

[10] - PP population in Children aged 3-11 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

### Primary: Geometric Mean Titer Ratios (GMTRs) of influenza Antibodies After Vaccination in subjects aged 12-17 years

|                 |                                                                                                                            |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|
| End point title | Geometric Mean Titer Ratios (GMTRs) of influenza Antibodies After Vaccination in subjects aged 12-17 years <sup>[11]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-hemagglutinin antibody titers were measured for each strain with the seroneutralization method. The GMTs were determined by HI titer.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

[11] - 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 analysis was performed based on the study group and the study vaccine administered for this outcome.

| End point values                         | Treatment              |  |  |  |
|------------------------------------------|------------------------|--|--|--|
| Subject group type                       | Reporting group        |  |  |  |
| Number of subjects analysed              | 60 <sup>[12]</sup>     |  |  |  |
| Units: Titer ratios (1/dil)              |                        |  |  |  |
| geometric mean (confidence interval 95%) |                        |  |  |  |
| A/H1N1                                   | 4.702 (3.595 to 6.151) |  |  |  |
| A/H3N2                                   | 5.993 (4.207 to 8.539) |  |  |  |
| B/                                       | 4.757 (3.762 to 6.014) |  |  |  |

Notes:

[12] - PP population in Children aged 12-17 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects Aged 3 to 11 Years With Seroprotection Against Influenza Antigens Before and After Vaccination

|                 |                                                                                                                                       |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects Aged 3 to 11 Years With Seroprotection Against Influenza Antigens Before and After Vaccination <sup>[13]</sup> |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-hemagglutinin antibody titers were measured for each strain with the seroneutralization method. Seroprotection was defined as antibody titers  $\geq 40$  (1/dil).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

[13] - 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 analysis was performed based on the study group and the study vaccine administered for this outcome.

| End point values              | Treatment          |  |  |  |
|-------------------------------|--------------------|--|--|--|
| Subject group type            | Reporting group    |  |  |  |
| Number of subjects analysed   | 60 <sup>[14]</sup> |  |  |  |
| Units: Percentage of subjects |                    |  |  |  |
| number (not applicable)       |                    |  |  |  |
| A/H1N1; Day 0                 | 50                 |  |  |  |
| A/H1N1; Day 21                | 91.67              |  |  |  |
| A/H3N2; Day 0                 | 70                 |  |  |  |
| A/H3N2; Day 21                | 95                 |  |  |  |
| B/; Day 0                     | 26.67              |  |  |  |
| B/; Day 21                    | 80                 |  |  |  |

Notes:

[14] - PP population in Children aged 3-11 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Subjects Aged 12-17 Years With Seroprotection Against Influenza Antigens Before and After Vaccination

|                 |                                                                                                                                     |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects Aged 12-17 Years With Seroprotection Against Influenza Antigens Before and After Vaccination <sup>[15]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-hemagglutinin antibody titers were measured for each strain with the seroneutralization method. Seroprotection was defined as antibody titers  $\geq 40$  (1/dil).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

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

Notes:

[15] - 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 analysis was performed based on the study group and the study vaccine administered for this outcome.

| End point values              | Treatment          |  |  |  |
|-------------------------------|--------------------|--|--|--|
| Subject group type            | Reporting group    |  |  |  |
| Number of subjects analysed   | 60 <sup>[16]</sup> |  |  |  |
| Units: Percentage of subjects |                    |  |  |  |
| number (not applicable)       |                    |  |  |  |
| A/H1N1; Day 0                 | 56.67              |  |  |  |
| A/H1N1; Day 21                | 96.67              |  |  |  |
| A/H3N2; Day 0                 | 58.33              |  |  |  |
| A/H3N2; Day 21                | 95                 |  |  |  |
| B/; Day 0                     | 40                 |  |  |  |
| B/; Day 21                    | 86.67              |  |  |  |

Notes:

[16] - PP population in Children aged 12-17 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

### Primary: Proportion of subjects seroconverted or had a significant increase in titres in subjects aged 3-11 years

|                 |                                                                                                                          |
|-----------------|--------------------------------------------------------------------------------------------------------------------------|
| End point title | Proportion of subjects seroconverted or had a significant increase in titres in subjects aged 3-11 years <sup>[17]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------------------|

End point description:

Criteria: number of seroconversions or significant increase in antihaemagglutinin antibody titre  $>40\%$

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:  
From day 0 to Day 21-28

Notes:

[17] - 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 analysis was performed based on the study group and the study vaccine administered for this outcome.

| End point values              | Treatment          |  |  |  |
|-------------------------------|--------------------|--|--|--|
| Subject group type            | Reporting group    |  |  |  |
| Number of subjects analysed   | 60 <sup>[18]</sup> |  |  |  |
| Units: Percentage of subjects |                    |  |  |  |
| number (not applicable)       |                    |  |  |  |
| A/H1N1                        | 61.67              |  |  |  |
| A/H3N2                        | 58.33              |  |  |  |
| B/                            | 66.67              |  |  |  |

Notes:

[18] - PP population in Children aged 3-11 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

## Primary: Increase in GMT in subjects aged 3-11 years

|                                                                               |                                                             |
|-------------------------------------------------------------------------------|-------------------------------------------------------------|
| End point title                                                               | Increase in GMT in subjects aged 3-11 years <sup>[19]</sup> |
| End point description:                                                        |                                                             |
| Criteria: mean geometric increase of antihaemagglutinin antibody titres: >2.5 |                                                             |
| End point type                                                                | Primary                                                     |
| End point timeframe:                                                          |                                                             |
| Day 0 to Day 21-28                                                            |                                                             |

Notes:

[19] - 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 analysis was performed based on the study group and the study vaccine administered for this outcome.

| End point values            | Treatment          |  |  |  |
|-----------------------------|--------------------|--|--|--|
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 60 <sup>[20]</sup> |  |  |  |
| Units: unit(s)              |                    |  |  |  |
| number (not applicable)     |                    |  |  |  |
| A/H1N1                      | 4.337              |  |  |  |
| A/H3N2                      | 4.982              |  |  |  |
| B/                          | 4.262              |  |  |  |

Notes:

[20] - PP population in Children aged 3-11 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

## Primary: Proportion of subjects seroprotected in subjects aged 3-11 years

|                                                                                                                                                                      |                                                                                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| End point title                                                                                                                                                      | Proportion of subjects seroprotected in subjects aged 3-11 years <sup>[21]</sup> |
| End point description:                                                                                                                                               |                                                                                  |
| Criteria: the proportion of subjects achieving an antihaemagglutinin antibody titre $\geq 40$ should be $>70\%$ .                                                    |                                                                                  |
| End point type                                                                                                                                                       | Primary                                                                          |
| End point timeframe:                                                                                                                                                 |                                                                                  |
| Day 0 to Day 21-28.                                                                                                                                                  |                                                                                  |
| Notes:                                                                                                                                                               |                                                                                  |
| [21] - 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 analysis was performed based on the study group and the study vaccine administered for this outcome.                                      |                                                                                  |

| End point values              | Treatment          |  |  |  |
|-------------------------------|--------------------|--|--|--|
| Subject group type            | Reporting group    |  |  |  |
| Number of subjects analysed   | 60 <sup>[22]</sup> |  |  |  |
| Units: Percentage of subjects |                    |  |  |  |
| number (not applicable)       |                    |  |  |  |
| A/H1N1                        | 91.67              |  |  |  |
| A/H3N2                        | 95                 |  |  |  |
| B/                            | 80                 |  |  |  |

Notes:

[22] - PP population in Children aged 3-11 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

## Primary: Proportion of subjects seroconverted or had a significant increase in titres in subjects aged 12-17 years

|                                                                                                                                                                      |                                                                                                                           |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                      | Proportion of subjects seroconverted or had a significant increase in titres in subjects aged 12-17 years <sup>[23]</sup> |
| End point description:                                                                                                                                               |                                                                                                                           |
| Criteria: number of seroconversions or significant increase in antihaemagglutinin antibody titre $>40\%$                                                             |                                                                                                                           |
| End point type                                                                                                                                                       | Primary                                                                                                                   |
| End point timeframe:                                                                                                                                                 |                                                                                                                           |
| Day 0 to Day 21-28.                                                                                                                                                  |                                                                                                                           |
| Notes:                                                                                                                                                               |                                                                                                                           |
| [23] - 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 analysis was performed based on the study group and the study vaccine administered for this outcome.                                      |                                                                                                                           |

| End point values              | Treatment          |  |  |  |
|-------------------------------|--------------------|--|--|--|
| Subject group type            | Reporting group    |  |  |  |
| Number of subjects analysed   | 60 <sup>[24]</sup> |  |  |  |
| Units: Percentage of subjects |                    |  |  |  |
| number (not applicable)       |                    |  |  |  |
| A/H1N1                        | 66.67              |  |  |  |
| A/H3N2                        | 61.67              |  |  |  |
| B/                            | 70                 |  |  |  |

Notes:

[24] - PP population in Children aged 12-17 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

### Primary: Increase in GMT in subjects aged 12-17 years

|                 |                                                              |
|-----------------|--------------------------------------------------------------|
| End point title | Increase in GMT in subjects aged 12-17 years <sup>[25]</sup> |
|-----------------|--------------------------------------------------------------|

End point description:

Criteria: mean geometric increase of antihaemagglutinin antibody titres: >2.5

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 0 to day 21-28.

Notes:

[25] - 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 analysis was performed based on the study group and the study vaccine administered for this outcome.

| End point values            | Treatment          |  |  |  |
|-----------------------------|--------------------|--|--|--|
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 60 <sup>[26]</sup> |  |  |  |
| Units: unit(s)              |                    |  |  |  |
| number (not applicable)     |                    |  |  |  |
| A/H1N1                      | 4.702              |  |  |  |
| A/H3N2                      | 5.993              |  |  |  |
| B/                          | 4.757              |  |  |  |

Notes:

[26] - PP population in Children aged 12-17 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

### Primary: Proportion of subjects seroprotected in subjects aged 12-17 years

|                 |                                                                                   |
|-----------------|-----------------------------------------------------------------------------------|
| End point title | Proportion of subjects seroprotected in subjects aged 12-17 years <sup>[27]</sup> |
|-----------------|-----------------------------------------------------------------------------------|

End point description:

Criteria: the proportion of subjects achieving an antihaemagglutinin antibody titre  $\geq 40$  should be  $>70\%$ .

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 0 to day 21-28.

Notes:

[27] - 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 analysis was performed based on the study group and the study vaccine administered for this outcome.

| <b>End point values</b>       | Treatment          |  |  |  |
|-------------------------------|--------------------|--|--|--|
| Subject group type            | Reporting group    |  |  |  |
| Number of subjects analysed   | 60 <sup>[28]</sup> |  |  |  |
| Units: Percentage of subjects |                    |  |  |  |
| number (not applicable)       |                    |  |  |  |
| A/H1N1                        | 96.67              |  |  |  |
| A/H3N2                        | 95                 |  |  |  |
| B/                            | 86.67              |  |  |  |

Notes:

[28] - PP population in Children aged 12-17 years: sixty (60) persons.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 0 to day 21-28.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |    |
|--------------------|----|
| Dictionary version | 14 |
|--------------------|----|

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Treatment group |
|-----------------------|-----------------|

Reporting group description: -

| <b>Serious adverse events</b>                     | Treatment group |  |  |
|---------------------------------------------------|-----------------|--|--|
| Total subjects affected by serious adverse events |                 |  |  |
| subjects affected / exposed                       | 0 / 120 (0.00%) |  |  |
| number of deaths (all causes)                     | 0               |  |  |
| number of deaths resulting from adverse events    | 0               |  |  |

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

| <b>Non-serious adverse events</b>                     | Treatment group                                                                                             |  |  |
|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|--|--|
| Total subjects affected by non-serious adverse events |                                                                                                             |  |  |
| subjects affected / exposed                           | 50 / 120 (41.67%)                                                                                           |  |  |
| Nervous system disorders                              |                                                                                                             |  |  |
| Headache                                              | Additional description: 1 of them was not related to the study medication, according to the investigator.   |  |  |
| subjects affected / exposed                           | 5 / 120 (4.17%)                                                                                             |  |  |
| occurrences (all)                                     | 5                                                                                                           |  |  |
| Syncope                                               | Additional description: All of them was not related to the study medication, according to the investigator. |  |  |
| subjects affected / exposed                           | 3 / 120 (2.50%)                                                                                             |  |  |
| occurrences (all)                                     | 3                                                                                                           |  |  |
| General disorders and administration site conditions  |                                                                                                             |  |  |
| Vaccination site pain                                 |                                                                                                             |  |  |
| subjects affected / exposed                           | 38 / 120 (31.67%)                                                                                           |  |  |
| occurrences (all)                                     | 38                                                                                                          |  |  |
| Vaccination site erythema                             |                                                                                                             |  |  |

|                                                 |                                                                                                             |  |  |
|-------------------------------------------------|-------------------------------------------------------------------------------------------------------------|--|--|
| subjects affected / exposed                     | 9 / 120 (7.50%)                                                                                             |  |  |
| occurrences (all)                               | 9                                                                                                           |  |  |
| Vaccination site induration                     |                                                                                                             |  |  |
| subjects affected / exposed                     | 8 / 120 (6.67%)                                                                                             |  |  |
| occurrences (all)                               | 8                                                                                                           |  |  |
| Vaccination site swelling                       |                                                                                                             |  |  |
| subjects affected / exposed                     | 9 / 120 (7.50%)                                                                                             |  |  |
| occurrences (all)                               | 9                                                                                                           |  |  |
| Vaccination site haematoma                      |                                                                                                             |  |  |
| subjects affected / exposed                     | 2 / 120 (1.67%)                                                                                             |  |  |
| occurrences (all)                               | 2                                                                                                           |  |  |
| Chills                                          | Additional description: 2 of them were not related to the study medication, according to the investigator.  |  |  |
| subjects affected / exposed                     | 3 / 120 (2.50%)                                                                                             |  |  |
| occurrences (all)                               | 3                                                                                                           |  |  |
| Malaise                                         | Additional description: 1 of them was not related to the study medication, according to the investigator.   |  |  |
| subjects affected / exposed                     | 9 / 120 (7.50%)                                                                                             |  |  |
| occurrences (all)                               | 9                                                                                                           |  |  |
| Pyrexia                                         | Additional description: 3 of them were not related to the study medication, according to the investigator.  |  |  |
| subjects affected / exposed                     | 6 / 120 (5.00%)                                                                                             |  |  |
| occurrences (all)                               | 6                                                                                                           |  |  |
| Immune system disorders                         |                                                                                                             |  |  |
| Hypersensitivity                                | Additional description: All of them was not related to the study medication, according to the investigator. |  |  |
| subjects affected / exposed                     | 1 / 120 (0.83%)                                                                                             |  |  |
| occurrences (all)                               | 1                                                                                                           |  |  |
| Gastrointestinal disorders                      |                                                                                                             |  |  |
| Vomiting                                        | Additional description: 1 of them was not related to the study medication, according to the investigator.   |  |  |
| subjects affected / exposed                     | 2 / 120 (1.67%)                                                                                             |  |  |
| occurrences (all)                               | 2                                                                                                           |  |  |
| Abdominal pain                                  |                                                                                                             |  |  |
| subjects affected / exposed                     | 1 / 120 (0.83%)                                                                                             |  |  |
| occurrences (all)                               | 1                                                                                                           |  |  |
| Respiratory, thoracic and mediastinal disorders |                                                                                                             |  |  |
| Oropharyngeal pain                              | Additional description: All of them was not related to the study medication, according to the investigator. |  |  |

|                                                 |                                                                                                             |  |  |
|-------------------------------------------------|-------------------------------------------------------------------------------------------------------------|--|--|
| subjects affected / exposed                     | 2 / 120 (1.67%)                                                                                             |  |  |
| occurrences (all)                               | 2                                                                                                           |  |  |
| Cough                                           | Additional description: All of them was not related to the study medication, according to the investigator. |  |  |
| subjects affected / exposed                     | 1 / 120 (0.83%)                                                                                             |  |  |
| occurrences (all)                               | 1                                                                                                           |  |  |
| Musculoskeletal and connective tissue disorders |                                                                                                             |  |  |
| Myalgia                                         |                                                                                                             |  |  |
| subjects affected / exposed                     | 12 / 120 (10.00%)                                                                                           |  |  |
| occurrences (all)                               | 12                                                                                                          |  |  |
| Infections and infestations                     |                                                                                                             |  |  |
| Nasopharyngitis                                 | Additional description: All of them was not related to the study medication, according to the investigator. |  |  |
| subjects affected / exposed                     | 1 / 120 (0.83%)                                                                                             |  |  |
| occurrences (all)                               | 1                                                                                                           |  |  |
| Pharyngitis                                     | Additional description: All of them was not related to the study medication, according to the investigator. |  |  |
| subjects affected / exposed                     | 1 / 120 (0.83%)                                                                                             |  |  |
| occurrences (all)                               | 1                                                                                                           |  |  |
| Cystitis                                        | Additional description: All of them was not related to the study medication, according to the investigator. |  |  |
| subjects affected / exposed                     | 1 / 120 (0.83%)                                                                                             |  |  |
| occurrences (all)                               | 1                                                                                                           |  |  |
| Helminthic infection                            | Additional description: All of them was not related to the study medication, according to the investigator. |  |  |
| subjects affected / exposed                     | 1 / 120 (0.83%)                                                                                             |  |  |
| occurrences (all)                               | 1                                                                                                           |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported