

**Clinical trial results:****A Randomized, Single-blind, Dose-Ranging Study to Evaluate Immunogenicity, Safety and Tolerability of Different Formulations of Adjuvanted and Nonadjuvanted Cell-derived, Inactivated Novel Swine Origin A/H1N1 Monovalent Subunit Influenza Virus Vaccine in Healthy Subjects from 6 Months to 17 Years of Age.****Summary**

| | |
|--------------------------|----------------|
| EudraCT number | 2009-013640-37 |
| Trial protocol | DE NL BE |
| Global end of trial date | 10 August 2011 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 28 July 2016 |
| First version publication date | 01 January 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Required for the re-QC project because of the EudraCT system glitch and possible updates to results may be required. Moreover, a change in system user for this study is necessary. |

Trial information**Trial identification**

| | |
|-----------------------|---------|
| Sponsor protocol code | V110_04 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00971100 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Novartis Vaccines and Diagnostics |
| Sponsor organisation address | Via Fiorentina 1, Siena, Italy, 53100 |
| Public contact | Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.com |
| Scientific contact | Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000663-PIP01-09 |
| 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? | Yes |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 16 November 2011 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 August 2011 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To identify the preferred vaccine formulation (with or without MF59), dosage (of antigen and adjuvant) and schedule (one or two administrations) of the cell-derived H1N1 swine (sw) monovalent vaccine in healthy children and adolescents based on CHMP criteria and pairwise statistical comparisons for immunogenicity, safety and tolerability.

Protection of trial subjects:

Study vaccines were not administered to individuals with known hypersensitivity to any component of the vaccines.

An oral temperature $\geq 38.0^{\circ}\text{C}$ ($\geq 100.4^{\circ}\text{F}$) or serious active infection was a reason for delaying vaccination.

Standard immunization practices were observed and care was taken to administer the injection intramuscularly. As with all injectable vaccines, appropriate medical treatment and supervision was readily available in case of rare anaphylactic reactions following administration of the study vaccine. Epinephrine 1:1000 and diphenhydramine was available in case of any anaphylactic reactions. Care was taken to ensure that the vaccine is not injected into a blood vessel.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------------|
| Actual start date of recruitment | 19 August 2009 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Scientific research |
| Long term follow-up duration | 18 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Netherlands: 10 |
| Country: Number of subjects enrolled | Belgium: 228 |
| Country: Number of subjects enrolled | Germany: 239 |
| Country: Number of subjects enrolled | Dominican Republic: 189 |
| Worldwide total number of subjects | 666 |
| EEA total number of subjects | 477 |

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) | 240 |
| Children (2-11 years) | 316 |
| Adolescents (12-17 years) | 110 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at seven sites in Germany, two sites in Belgium, one site in the Netherlands, two sites in Dominican Republic

Pre-assignment

Screening details:

Subjects were enrolled in an age-descending manner and stratified into 4 age cohorts: 9 to 17 years (cohort 1), 3 to 8 years (cohort 2), 12 to 35 months (cohort 3), and 6 to 11 months (cohort 4).

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Subject |

Arms

| | |
|------------------------------|---------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cohort 1 (3.75_Half MF59) |

Arm description:

Subjects aged ≥ 9 to ≤ 17 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an adjuvanted trivalent influenza vaccine (aTIV).

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | H1N1 Vaccine |
| Investigational medicinal product code | V110 |
| Other name | FCC-H1N1sw |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Vaccination consisted of two 0.25 mL doses of H1N1 vaccine (3.75mcg of H1N1 and half MF59) administered 3 weeks apart followed by one dose of 0.5mL booster vaccination with aTIV; all injections were administered IM in the deltoid muscle preferably of the non-dominant arm.

| | |
|------------------|--------------------------|
| Arm title | Cohort 1 (7.5_Full MF59) |
|------------------|--------------------------|

Arm description:

Subjects aged ≥ 9 to ≤ 17 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | H1N1 Vaccine |
| Investigational medicinal product code | V110 |
| Other name | FCC-H1N1sw |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Vaccination consisted of two 0.5 mL doses of H1N1 vaccine (7.5mcg of H1N1 and full MF59) administered 3 weeks apart followed by one dose of 0.5mL booster vaccination with aTIV; all injections were administered IM in the deltoid muscle preferably of the non-dominant arm.

| | |
|------------------|---------------------------|
| Arm title | Cohort 2 (3.75_Half MF59) |
|------------------|---------------------------|

Arm description:

Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed

by a booster dose 12 months after first vaccination with an aTIV.

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | H1N1 Vaccine |
| Investigational medicinal product code | V110 |
| Other name | FCC-H1N1sw |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Vaccination consisted of two 0.25 mLdoses of H1N1 vaccine (3.75mcg of H1N1 and half MF59) administered 3 weeks apart followed by one dose of 0.5mL booster vaccination with aTIV; all injections were administered IM in the deltoid muscle preferably of the non-dominant arm.

| | |
|------------------|--------------------------|
| Arm title | Cohort 2 (7.5_Full MF59) |
|------------------|--------------------------|

Arm description:

Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | H1N1 Vaccine |
| Investigational medicinal product code | V110 |
| Other name | FCC-H1N1sw |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Vaccination consisted of two 0.5 mLdoses of H1N1 vaccine (7.5mcg of H1N1 and full MF59) administered 3 weeks apart followed by one dose of 0.5mL booster vaccination with aTIV; all injections were administered IM in the deltoid muscle preferably of the non-dominant arm.

| | |
|------------------|-----------------------|
| Arm title | Cohort 2 (15_No MF59) |
|------------------|-----------------------|

Arm description:

Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | H1N1 Vaccine |
| Investigational medicinal product code | V110 |
| Other name | FCC-H1N1sw |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Vaccination consisted of two 0.5 mLdoses of H1N1 vaccine (15mcg of H1N1 without MF59) administered 3 weeks apart followed by one dose of 0.5mL booster vaccination with aTIV; all injections were administered IM in the deltoid muscle preferably of the non-dominant arm.

| | |
|------------------|---------------------------|
| Arm title | Cohort 3 (3.75_Half MF59) |
|------------------|---------------------------|

Arm description:

Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | H1N1 Vaccine |
| Investigational medicinal product code | V110 |
| Other name | FCC-H1N1sw |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Vaccination consisted of two 0.25 mLdoses of H1N1 vaccine (3.75mcg of H1N1 and half MF59) administered 3 weeks apart followed by one dose of 0.5mL booster vaccination with aTIV; all injections were administered IM in the deltoid muscle preferably of the non-dominant arm for subjects ≥ 24 months of age. For subjects aged ≤ 24 months, the injections were administered in the anterolateral aspect of thigh.

| | |
|---|---------------------------|
| Arm title | Cohort 3 (7.5_Full MF59) |
| Arm description: Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Arm type | Experimental |
| Investigational medicinal product name | H1N1 Vaccine |
| Investigational medicinal product code | V110 |
| Other name | FCC-H1N1sw |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: Vaccination consisted of two 0.5 mLdoses of H1N1 vaccine (7.5mcg of H1N1 and full MF59) administered 3 weeks apart followed by one dose of 0.5mL booster vaccination with aTIV; all injections were administered IM in the deltoid muscle preferably of the non-dominant arm for subjects ≥ 24 months of age. For subjects aged ≤ 24 months, the injections were administered in the anterolateral aspect of thigh. | |
| Arm title | Cohort 3 (15_No MF59) |
| Arm description: Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Arm type | Experimental |
| Investigational medicinal product name | H1N1 Vaccine |
| Investigational medicinal product code | V110 |
| Other name | FCC-H1N1sw |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: Vaccination consisted of two 0.5 mLdoses of H1N1 vaccine (15mcg of H1N1 without MF59) administered 3 weeks apart followed by one dose of 0.5mL booster vaccination with aTIV; all injections were administered IM in the deltoid muscle preferably of the non-dominant arm for subjects ≥ 24 months of age. For subjects aged ≤ 24 months, the injections were administered in the anterolateral aspect of thigh. | |
| Arm title | Cohort 4 (3.75_Half MF59) |
| Arm description: Subjects aged ≥ 6 to ≤ 11 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Arm type | Experimental |
| Investigational medicinal product name | H1N1 Vaccine |
| Investigational medicinal product code | V110 |
| Other name | FCC-H1N1sw |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: Vaccination consisted of two 0.25 mLdoses of H1N1 vaccine (3.75mcg of H1N1 and half MF59) administered 3 weeks apart followed by one dose of 0.5mL booster vaccination with aTIV. For subjects aged ≤ 24 months, the injections were administered in the anterolateral aspect of thigh. | |
| Arm title | Cohort 4 (7.5_Full MF59) |
| Arm description: Subjects aged ≥ 6 to ≤ 11 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Arm type | Experimental |

| | |
|--|--------------------------|
| Investigational medicinal product name | H1N1 Vaccine |
| Investigational medicinal product code | V110 |
| Other name | FCC-H1N1sw |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Vaccination consisted of two 0.5 mL doses of H1N1 vaccine (7.5mcg of H1N1 and full MF59) administered 3 weeks apart followed by one dose of 0.5mL booster vaccination with aTIV. For subjects aged ≤ 24 months, the injections were administered in the anterolateral aspect of thigh.

| Number of subjects in period 1 | Cohort 1 (3.75_Half MF59) | Cohort 1 (7.5_Full MF59) | Cohort 2 (3.75_Half MF59) |
|---------------------------------------|---------------------------|--------------------------|---------------------------|
| Started | 80 | 79 | 72 |
| Completed | 23 | 24 | 30 |
| Not completed | 57 | 55 | 42 |
| Consent withdrawn by subject | 5 | 3 | 4 |
| Adverse Event | 2 | - | - |
| Administrative Reason | 48 | 51 | 32 |
| Lost to follow-up | 1 | 1 | 5 |
| Unable to Classify | - | - | 1 |
| Protocol deviation | 1 | - | - |

| Number of subjects in period 1 | Cohort 2 (7.5_Full MF59) | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half MF59) |
|---------------------------------------|--------------------------|-----------------------|---------------------------|
| Started | 73 | 39 | 65 |
| Completed | 35 | 14 | 41 |
| Not completed | 38 | 25 | 24 |
| Consent withdrawn by subject | 7 | 8 | 8 |
| Adverse Event | 1 | 1 | 1 |
| Administrative Reason | 30 | 13 | 11 |
| Lost to follow-up | - | 3 | 4 |
| Unable to Classify | - | - | - |
| Protocol deviation | - | - | - |

| Number of subjects in period 1 | Cohort 3 (7.5_Full MF59) | Cohort 3 (15_No MF59) | Cohort 4 (3.75_Half MF59) |
|---------------------------------------|--------------------------|-----------------------|---------------------------|
| Started | 73 | 34 | 75 |
| Completed | 49 | 21 | 66 |
| Not completed | 24 | 13 | 9 |
| Consent withdrawn by subject | 11 | 3 | 4 |
| Adverse Event | - | 1 | 1 |
| Administrative Reason | 10 | 5 | 3 |
| Lost to follow-up | 2 | 2 | 1 |
| Unable to Classify | - | 1 | - |

| | | | |
|--------------------|---|---|---|
| Protocol deviation | 1 | 1 | - |
|--------------------|---|---|---|

| Number of subjects in period 1 | Cohort 4 (7.5_Full MF59) |
|---------------------------------------|--------------------------|
| Started | 76 |
| Completed | 61 |
| Not completed | 15 |
| Consent withdrawn by subject | 9 |
| Adverse Event | 1 |
| Administrative Reason | 4 |
| Lost to follow-up | - |
| Unable to Classify | 1 |
| Protocol deviation | - |

Baseline characteristics

Reporting groups

| | |
|--|---------------------------|
| Reporting group title | Cohort 1 (3.75_Half MF59) |
| Reporting group description: | |
| Subjects aged ≥ 9 to ≤ 17 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an adjuvanted trivalent influenza vaccine (aTIV). | |
| Reporting group title | Cohort 1 (7.5_Full MF59) |
| Reporting group description: | |
| Subjects aged ≥ 9 to ≤ 17 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 2 (3.75_Half MF59) |
| Reporting group description: | |
| Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 2 (7.5_Full MF59) |
| Reporting group description: | |
| Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 2 (15_No MF59) |
| Reporting group description: | |
| Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 3 (3.75_Half MF59) |
| Reporting group description: | |
| Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 3 (7.5_Full MF59) |
| Reporting group description: | |
| Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 3 (15_No MF59) |
| Reporting group description: | |
| Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 4 (3.75_Half MF59) |
| Reporting group description: | |
| Subjects aged ≥ 6 to ≤ 11 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 4 (7.5_Full MF59) |
| Reporting group description: | |
| Subjects aged ≥ 6 to ≤ 11 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |

| Reporting group values | Cohort 1 (3.75_Half MF59) | Cohort 1 (7.5_Full MF59) | Cohort 2 (3.75_Half MF59) |
|--|---------------------------|--------------------------|---------------------------|
| Number of subjects | 80 | 79 | 72 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |

| | | | |
|---|---------------|---------------|--------------|
| Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: months arithmetic mean standard deviation | 13.2 ± 2.7 | 13.2 ± 2.7 | 5.5 ± 1.9 |
| Gender categorical Units: Subjects | | | |
| Female | 41 | 37 | 45 |
| Male | 39 | 42 | 27 |

| Reporting group values | Cohort 2 (7.5_Full MF59) | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half MF59) |
|---|--------------------------|-----------------------|---------------------------|
| Number of subjects | 73 | 39 | 65 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: months arithmetic mean standard deviation | 5.3 ± 1.7 | 5.2 ± 1.5 | 21.8 ± 7.3 |
| Gender categorical Units: Subjects | | | |
| Female | 31 | 25 | 34 |
| Male | 42 | 14 | 31 |

| Reporting group values | Cohort 3 (7.5_Full MF59) | Cohort 3 (15_No MF59) | Cohort 4 (3.75_Half MF59) |
|---|--------------------------|-----------------------|---------------------------|
| Number of subjects | 73 | 34 | 75 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) | | | |

| | | | |
|---------------------------|-------|-------|-------|
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age continuous | | | |
| Units: months | | | |
| arithmetic mean | 23.1 | 23.1 | 8.9 |
| standard deviation | ± 7.1 | ± 7.8 | ± 1.5 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 27 | 14 | 40 |
| Male | 46 | 20 | 35 |

| Reporting group values | Cohort 4 (7.5_Full MF59) | Total | |
|--|--------------------------|-------|--|
| Number of subjects | 76 | 666 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 0 | |
| Newborns (0-27 days) | | 0 | |
| Infants and toddlers (28 days-23 months) | | 0 | |
| Children (2-11 years) | | 0 | |
| Adolescents (12-17 years) | | 0 | |
| Adults (18-64 years) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: months | | | |
| arithmetic mean | 8.8 | | |
| standard deviation | ± 1.7 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 42 | 336 | |
| Male | 34 | 330 | |

End points

End points reporting groups

| | |
|--|---------------------------|
| Reporting group title | Cohort 1 (3.75_Half MF59) |
| Reporting group description: Subjects aged ≥ 9 to ≤ 17 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an adjuvanted trivalent influenza vaccine (aTIV). | |
| Reporting group title | Cohort 1 (7.5_Full MF59) |
| Reporting group description: Subjects aged ≥ 9 to ≤ 17 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 2 (3.75_Half MF59) |
| Reporting group description: Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 2 (7.5_Full MF59) |
| Reporting group description: Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 2 (15_No MF59) |
| Reporting group description: Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 3 (3.75_Half MF59) |
| Reporting group description: Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 3 (7.5_Full MF59) |
| Reporting group description: Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 3 (15_No MF59) |
| Reporting group description: Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 4 (3.75_Half MF59) |
| Reporting group description: Subjects aged ≥ 6 to ≤ 11 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Reporting group title | Cohort 4 (7.5_Full MF59) |
| Reporting group description: Subjects aged ≥ 6 to ≤ 11 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV. | |
| Subject analysis set title | Per protocol set- day 366 |
| Subject analysis set type | Per protocol |
| Subject analysis set description: All subjects who received all the relevant doses of vaccine correctly and provided evaluable serum samples at relevant time points (day 366) and who had no major protocol violations as pre-specified in the analysis plan | |
| Subject analysis set title | Per protocol set- day 387 |
| Subject analysis set type | Per protocol |
| Subject analysis set description: All subjects who received all the relevant doses of vaccine correctly and provided evaluable serum | |

samples at relevant time points (day 387) and who had no major protocol violations as pre-specified in the analysis plan

| | |
|----------------------------|--------------------------|
| Subject analysis set title | Per protocol set- Day 43 |
|----------------------------|--------------------------|

| | |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

All subjects who received all the relevant doses of vaccine correctly and provided evaluable serum samples at relevant time points (day 43) and who had no major protocol violations as pre-specified in the analysis plan

| | |
|----------------------------|------------|
| Subject analysis set title | Safety Set |
|----------------------------|------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

All subjects in the All Exposed Set who provided post-baseline safety data.

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | All Cohorts (7.5_Full MF59) |
|----------------------------|-----------------------------|

| | |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

Subjects from all the cohorts receiving H1N1 vaccine (7.5 mcg+full MF59) were pooled.

| | |
|----------------------------|------------------------------|
| Subject analysis set title | All Cohorts (3.75_Half MF59) |
|----------------------------|------------------------------|

| | |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

Subjects from all the cohorts receiving H1N1 vaccine (3.75 mcg+half MF59) were pooled.

Primary: 1. Percentages of subjects achieving seroconversion against A/H1N1 Strain as measured by hemagglutination inhibition (HI) assay.

| | |
|-----------------|--|
| End point title | 1. Percentages of subjects achieving seroconversion against A/H1N1 Strain as measured by hemagglutination inhibition (HI) assay. |
|-----------------|--|

End point description:

Immunogenicity was measured in terms of percentage of subjects achieving seroconversion or significant increase in HI titer against the vaccine strain, 3 weeks after receiving 2 doses of vaccination according to CHMP criterion.

Seroconversion is defined as HI ≥ 40 for subjects negative at baseline [<10] or at least 4-fold increase in HI titer for those positive at baseline [≥ 10] on day 22 and day 43.

There are no predefined CHMP criteria for the pediatric population however, the criterion is met if the percentage of subjects achieving seroconversion or at least 4-fold increase in HI antibody (at day 43) is $>40\%$.

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

End point timeframe:

Day 43 (3 weeks post second vaccination)

| End point values | Cohort 1 (3.75_Half) | Cohort 1 (7.5_Full) | Cohort 2 (3.75_Half) | Cohort 2 (7.5_Full) |
|----------------------------------|-------------------------|------------------------|-------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 72 | 71 | 58 | 60 |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 43 | 99 (93 to 100) | 100 (95 to 100) | 100 (94 to 100) | 100 (94 to 100) |

| End point values | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half) | Cohort 3 (7.5_Full) | Cohort 3 (15_No MF59) |
|----------------------------------|--------------------------|-------------------------|------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 31 | 51 | 53 | 25 |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 43 | 97 (83 to 100) | 98 (90 to 100) | 100 (93 to 100) | 84 (64 to 95) |

| End point values | Cohort 4 (3.75_Half) | Cohort 4 (7.5_Full) | | |
|----------------------------------|-------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 58 | 54 | | |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 43 | 98 (91 to 100) | 100 (93 to 100) | | |

Statistical analyses

| Statistical analysis title | Cohort 1: 3.75_Half MF59 vs 7.5_Full MF59 |
|--|--|
| Statistical analysis description: The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated. | |
| Comparison groups | Cohort 1 (7.5_Full MF59) v Cohort 1 (3.75_Half MF59) |
| Number of subjects included in analysis | 143 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group differences |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4 |
| upper limit | 1 |

| Statistical analysis title | Cohort 2: 3.75_Half MF59 vs 7.5_Full MF59 |
|---|--|
| Statistical analysis description: The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated | |
| Comparison groups | Cohort 2 (3.75_Half MF59) v Cohort 2 (7.5_Full MF59) |

| | |
|---|----------------------|
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Cohort 2: 3.75_Half MF59 vs 15_No MF59 |
|-----------------------------------|--|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|---|---|
| Comparison groups | Cohort 2 (3.75_Half MF59) v Cohort 2 (15_No MF59) |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | 9 |

| | |
|-----------------------------------|---------------------------------------|
| Statistical analysis title | Cohort 2: 7.5_Full MF59 vs 15_No MF59 |
|-----------------------------------|---------------------------------------|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|---|--|
| Comparison groups | Cohort 2 (7.5_Full MF59) v Cohort 2 (15_No MF59) |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | 9 |

| | |
|---|--|
| Statistical analysis title | Cohort 3: 3.75_Half MF59 vs 7.5_Full MF59 |
| Statistical analysis description: The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated | |
| Comparison groups | Cohort 3 (3.75_Half MF59) v Cohort 3 (7.5_Full MF59) |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | -2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6 |
| upper limit | 2 |

| | |
|---|---|
| Statistical analysis title | Cohort 3: 3.75_Half MF59 vs 15_No MF59 |
| Statistical analysis description: The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated | |
| Comparison groups | Cohort 3 (3.75_Half MF59) v Cohort 3 (15_No MF59) |
| Number of subjects included in analysis | 76 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 29 |

| | |
|---|--|
| Statistical analysis title | Cohort 3: 7.5_Full MF59 vs 15_No MF59 |
| Statistical analysis description: The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated | |
| Comparison groups | Cohort 3 (7.5_Full MF59) v Cohort 3 (15_No MF59) |

| | |
|---|----------------------|
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 16 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2 |
| upper limit | 30 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Cohort 4: 3.75_Half MF59 vs 7.5_Full MF59 |
|-----------------------------------|---|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|---|--|
| Comparison groups | Cohort 4 (3.75_Half MF59) v Cohort 4 (7.5_Full MF59) |
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | -2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 2 |

Primary: 2. Percentages of subjects achieving HI titers $\geq 1:40$ against A/H1N1 Strain.

| | |
|-----------------|---|
| End point title | 2. Percentages of subjects achieving HI titers $\geq 1:40$ against A/H1N1 Strain. |
|-----------------|---|

End point description:

Immunogenicity was measured in terms of percentage of subjects achieving HI titers $\geq 1:40$ against A/H1N1 strain, 3 weeks after receiving 2 doses of vaccination according to CHMP criterion.

There are no predefined CHMP criteria for the pediatric population however, the criterion is met if the percentage of subjects achieving HI antibody titer $\geq 1:40$ is $>70\%$ (at day 43).

| | |
|--|---------|
| End point type | Primary |
| End point timeframe: | |
| Day 43 (3 weeks post second vaccination) | |

| End point values | Cohort 1 (3.75_Half) | Cohort 1 (7.5_Full) | Cohort 2 (3.75_Half) | Cohort 2 (7.5_Full) |
|----------------------------------|-------------------------|------------------------|-------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 72 | 71 | 58 | 60 |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 1 | 6 (2 to 14) | 3 (0 to 10) | 0 (0 to 6) | 2 (0.042 to 9) |
| Day 43 | 100 (95 to 100) | 100 (95 to 100) | 100 (94 to 100) | 100 (94 to 100) |

| End point values | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half) | Cohort 3 (7.5_Full) | Cohort 3 (15_No MF59) |
|----------------------------------|--------------------------|-------------------------|------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 31 | 51 | 53 | 25 |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 1 | 0 (0 to 11) | 12 (4 to 24) | 13 (5 to 25) | 20 (7 to 41) |
| Day 43 | 97 (83 to 100) | 100 (93 to 100) | 100 (93 to 100) | 88 (69 to 97) |

| End point values | Cohort 4 (3.75_Half) | Cohort 4 (7.5_Full) | | |
|----------------------------------|-------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 58 | 54 | | |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 1 | 17 (9 to 29) | 17 (8 to 29) | | |
| Day 43 | 100 (94 to 100) | 100 (93 to 100) | | |

Statistical analyses

| Statistical analysis title | Cohort 1: 3.75_Half MF59 vs 7.5_Full MF59 |
|--|--|
| Statistical analysis description: | |
| The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated | |
| Comparison groups | Cohort 1 (3.75_Half MF59) v Cohort 1 (7.5_Full MF59) |
| Number of subjects included in analysis | 143 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group differences |
| Point estimate | 0 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Cohort 2: 3.75_Half MF59 vs 7.5_Full MF59 |
|-----------------------------------|---|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|---|--|
| Comparison groups | Cohort 2 (3.75_Half MF59) v Cohort 2 (7.5_Full MF59) |
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Cohort 2: 3.75_Half MF59 vs 15_No MF59 |
|-----------------------------------|--|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|---|---|
| Comparison groups | Cohort 2 (15_No MF59) v Cohort 2 (3.75_Half MF59) |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | 9 |

| | |
|-----------------------------------|---------------------------------------|
| Statistical analysis title | Cohort 2: 7.5_Full MF59 vs 15_No MF59 |
|-----------------------------------|---------------------------------------|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|-------------------|--|
| Comparison groups | Cohort 2 (7.5_Full MF59) v Cohort 2 (15_No MF59) |
|-------------------|--|

| | |
|---|----------------------|
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | 9 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Cohort 3: 3.75_Half MF59 vs 7.5_Full MF59 |
|-----------------------------------|---|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|---|--|
| Comparison groups | Cohort 3 (3.75_Half MF59) v Cohort 3 (7.5_Full MF59) |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Cohort 3: 3.75_Half MF59 vs 15_No MF59 |
|-----------------------------------|--|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|---|---|
| Comparison groups | Cohort 3 (3.75_Half MF59) v Cohort 3 (15_No MF59) |
| Number of subjects included in analysis | 76 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 25 |

| | |
|---|--|
| Statistical analysis title | Cohort 3: 7.5_Full MF59 vs 15_No MF59 |
| Statistical analysis description: The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated | |
| Comparison groups | Cohort 3 (7.5_Full MF59) v Cohort 3 (15_No MF59) |
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 25 |

| | |
|---|--|
| Statistical analysis title | Cohort 4: 3.75_Half MF59 vs 7.5_Full MF59 |
| Statistical analysis description: The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated | |
| Comparison groups | Cohort 4 (3.75_Half MF59) v Cohort 4 (7.5_Full MF59) |
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0 |

Primary: 3. Geometric mean ratios against A/H1N1 strain following 2-dose vaccination schedule as determined by HI assay

| | |
|-----------------|--|
| End point title | 3. Geometric mean ratios against A/H1N1 strain following 2-dose vaccination schedule as determined by HI assay |
|-----------------|--|

End point description:

Immunogenicity was measured in terms of geometric mean ratios. The ratio of postvaccination to prevaccination HI GMTs, 3 weeks after second vaccination was reported.

There are no predefined CHMP criteria for the pediatric population however, the criterion is met if the geometric mean ratio (day 43/day 1) in HI antibody titer is >2.5.

| | |
|--|---------|
| End point type | Primary |
| End point timeframe: | |
| Day 1 and Day 43 (3 weeks post second vaccination) | |

| End point values | Cohort 1 (3.75_Half) | Cohort 1 (7.5_Full) | Cohort 2 (3.75_Half) | Cohort 2 (7.5_Full) |
|--|-------------------------|------------------------|-------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 72 | 71 | 58 | 60 |
| Units: Ratios | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 43/Day 1 | 47 (36 to 61) | 80 (61 to 103) | 86 (67 to 111) | 115 (91 to 147) |

| End point values | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half) | Cohort 3 (7.5_Full) | Cohort 3 (15_No MF59) |
|--|--------------------------|-------------------------|------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 31 | 51 | 53 | 25 |
| Units: Ratios | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 43/Day 1 | 28 (21 to 38) | 89 (54 to 145) | 108 (69 to 169) | 11 (6.23 to 20) |

| End point values | Cohort 4 (3.75_Half) | Cohort 4 (7.5_Full) | | |
|--|-------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 58 | 54 | | |
| Units: Ratios | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 43/Day 1 | 92 (51 to 166) | 129 (72 to 232) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Cohort 1: 3.75_Half MF59 vs 7.5_Full MF59 |
| Statistical analysis description: | |
| The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated | |
| Comparison groups | Cohort 1 (3.75_Half MF59) v Cohort 1 (7.5_Full MF59) |

| | |
|---|----------------------|
| Number of subjects included in analysis | 143 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 0.59 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.42 |
| upper limit | 0.82 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Cohort 2: 3.75_Half MF59 vs 7.5_Full MF59 |
|-----------------------------------|---|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|---|--|
| Comparison groups | Cohort 2 (3.75_Half MF59) v Cohort 2 (7.5_Full MF59) |
| Number of subjects included in analysis | 118 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.56 |
| upper limit | 1 |

| | |
|-----------------------------------|-----------------------------------|
| Statistical analysis title | Cohort 2: 3.75_MF59 vs 15_No MF59 |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|---|---|
| Comparison groups | Cohort 2 (3.75_Half MF59) v Cohort 2 (15_No MF59) |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 3.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.16 |
| upper limit | 4.35 |

| | |
|---|--|
| Statistical analysis title | Cohort 2: 7.5_Full MF59 vs 15_no MF59 |
| Statistical analysis description: The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated | |
| Comparison groups | Cohort 2 (7.5_Full MF59) v Cohort 2 (15_No MF59) |
| Number of subjects included in analysis | 91 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 4.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.91 |
| upper limit | 5.81 |

| | |
|---|--|
| Statistical analysis title | Cohort 3: 3.75_Half MF59 vs 7.5_Full MF59 |
| Statistical analysis description: The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated | |
| Comparison groups | Cohort 3 (3.75_Half MF59) v Cohort 3 (7.5_Full MF59) |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.53 |
| upper limit | 1.29 |

| | |
|---|---|
| Statistical analysis title | Cohort 3: 3.75_Half MF59 vs 15_No MF59 |
| Statistical analysis description: The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated | |
| Comparison groups | Cohort 3 (15_No MF59) v Cohort 3 (3.75_Half MF59) |

| | |
|---|----------------------|
| Number of subjects included in analysis | 76 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 7.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.53 |
| upper limit | 14 |

| | |
|-----------------------------------|---------------------------------------|
| Statistical analysis title | Cohort 3: 7.5_Full MF59 vs 15_No MF59 |
|-----------------------------------|---------------------------------------|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|---|--|
| Comparison groups | Cohort 3 (7.5_Full MF59) v Cohort 3 (15_No MF59) |
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 9.59 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.51 |
| upper limit | 17 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Cohort 4: 3.75_Half MF59 vs 7.5_Full MF59 |
|-----------------------------------|---|

Statistical analysis description:

The statistical significance for the differences in immune responses between vaccine groups on day 43 was calculated

| | |
|---|--|
| Comparison groups | Cohort 4 (3.75_Half MF59) v Cohort 4 (7.5_Full MF59) |
| Number of subjects included in analysis | 112 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | ANOVA |
| Parameter estimate | Vaccine group ratios |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.48 |
| upper limit | 1.08 |

Primary: 4. Number of Subjects Reporting Solicited Local and Systemic Adverse Events, After Any Primary Vaccination

| | |
|-----------------|---|
| End point title | 4. Number of Subjects Reporting Solicited Local and Systemic Adverse Events, After Any Primary Vaccination ^[1] |
|-----------------|---|

End point description:

Safety was assessed as the number of subjects who reported solicited local and systemic adverse events, 3 weeks after the primary course with H1N1sw monovalent vaccine.

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

End point timeframe:

From day 1 through day 7 after any 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: No statistical analyses for this end point

| End point values | Cohort 1 (3.75_Half | Cohort 1 (7.5_Full | Cohort 2 (3.75_Half | Cohort 2 (7.5_Full |
|--|------------------------|-----------------------|------------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 79 | 79 | 71 | 72 |
| Units: Number | | | | |
| Ecchymosis (N=79,79,71,72,39,65,73,33,75,74) | 5 | 7 | 9 | 9 |
| Erythema (N=79,79,71,72,39,65,73,33,75,74) | 10 | 16 | 14 | 23 |
| Induration (N=79,79,71,72,39,65,73,33,75,74) | 13 | 15 | 8 | 16 |
| Swelling (N=79,79,71,72,39,65,73,33,75,74) | 9 | 13 | 9 | 11 |
| Tenderness (N=0,0,0,0,0,65,73,33,75,74) | 0 | 0 | 0 | 0 |
| Pain (N=79,79,70,72,39,65,73,33,75,74) | 61 | 67 | 39 | 40 |
| Chills (N=79,79,70,72,39,0,0,0,0,0) | 3 | 10 | 3 | 7 |
| Malaise (N=79,79,70,72,39,0,0,0,0,0) | 10 | 16 | 12 | 5 |
| Myalgia (N=79,79,70,72,39,0,0,0,0,0) | 21 | 21 | 6 | 10 |
| Arthralgia (N=79,79,70,72,39,0,0,0,0,0) | 12 | 10 | 5 | 6 |
| Headache (N=79,79,70,72,39,0,0,0,0,0) | 22 | 25 | 7 | 8 |
| Sweating (N=79,79,70,72,39,0,0,0,0,0) | 5 | 3 | 1 | 1 |
| Fatigue (N=79,79,70,72,39,0,0,0,0,0) | 23 | 25 | 21 | 17 |
| Nausea(N=79,79,70,72,39,0,0,0,0,0) | 9 | 8 | 5 | 6 |
| Diarrhea (N=0,0,0,0,0,65,73,33,75,74) | 0 | 0 | 0 | 0 |
| Sleepiness (N=0,0,0,0,0,65,73,33,75,74) | 0 | 0 | 0 | 0 |
| Vomiting (N=0,0,0,0,0,65,73,33,75,74) | 0 | 0 | 0 | 0 |
| Irritability (N=0,0,0,0,0,65,73,33,75,74) | 0 | 0 | 0 | 0 |
| Chang. eating habits (N=0,0,0,0,0,65,73,33,75,74) | 0 | 0 | 0 | 0 |
| Unus. Crying (N=0,0,0,0,0,65,73,33,75,74) | 0 | 0 | 0 | 0 |
| Shivering (N=0,0,0,0,0,65,73,33,75,74) | 0 | 0 | 0 | 0 |

| | | | | |
|--|----|----|----|----|
| Fever ($\geq 38^{\circ}\text{C}$) (N=79,79,70,72,39,65,73,33,75,74) | 2 | 1 | 10 | 7 |
| Temp ($\geq 40^{\circ}\text{C}$) (N=79,79,70,72,39,65,73,33,75,74) | 0 | 0 | 0 | 0 |
| Stayed Home (N=79,79,70,72,39,65,73,33,75,74) | 4 | 3 | 5 | 13 |
| Analg.Antipy Used (N=79,79,70,72,39,65,73,33,75,74) | 11 | 12 | 11 | 16 |

| End point values | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half) | Cohort 3 (7.5_Full) | Cohort 3 (15_No MF59) |
|--|--------------------------|-------------------------|------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 39 | 65 | 71 | 33 |
| Units: Number | | | | |
| Ecchymosis (N=79,79,71,72,39,65,73,33,75,74) | 10 | 4 | 10 | 5 |
| Erythema (N=79,79,71,72,39,65,73,33,75,74) | 8 | 13 | 17 | 8 |
| Induration (N=79,79,71,72,39,65,73,33,75,74) | 6 | 8 | 13 | 5 |
| Swelling (N=79,79,71,72,39,65,73,33,75,74) | 4 | 2 | 7 | 3 |
| Tenderness (N=0,0,0,0,0,65,73,33,75,74) | 0 | 9 | 36 | 13 |
| Pain (N=79,79,70,72,39,65,73,33,75,74) | 19 | 0 | 0 | 0 |
| Chills (N=79,79,70,72,39,0,0,0,0,0) | 2 | 0 | 0 | 0 |
| Malaise (N=79,79,70,72,39,0,0,0,0,0) | 7 | 0 | 0 | 0 |
| Myalgia (N=79,79,70,72,39,0,0,0,0,0) | 3 | 0 | 0 | 0 |
| Arthralgia (N=79,79,70,72,39,0,0,0,0,0) | 2 | 0 | 0 | 0 |
| Headache (N=79,79,70,72,39,0,0,0,0,0) | 6 | 0 | 0 | 0 |
| Sweating (N=79,79,70,72,39,0,0,0,0,0) | 0 | 0 | 0 | 0 |
| Fatigue (N=79,79,70,72,39,0,0,0,0,0) | 8 | 0 | 0 | 0 |
| Nausea(N=79,79,70,72,39,0,0,0,0,0) | 3 | 0 | 0 | 0 |
| Diarrhea (N=0,0,0,0,0,65,73,33,75,74) | 0 | 21 | 24 | 8 |
| Sleepiness (N=0,0,0,0,0,65,73,33,75,74) | 0 | 17 | 30 | 9 |
| Vomiting (N=0,0,0,0,0,65,73,33,75,74) | 0 | 11 | 18 | 3 |
| Irritability (N=0,0,0,0,0,65,73,33,75,74) | 0 | 19 | 18 | 7 |
| Chang. eating habits (N=0,0,0,0,0,65,73,33,75,74) | 0 | 21 | 26 | 6 |
| Unus. Crying (N=0,0,0,0,0,65,73,33,75,74) | 0 | 20 | 27 | 10 |
| Shivering (N=0,0,0,0,0,65,73,33,75,74) | 0 | 6 | 6 | 2 |
| Fever ($\geq 38^{\circ}\text{C}$) (N=79,79,70,72,39,65,73,33,75,74) | 3 | 17 | 12 | 5 |
| Temp ($\geq 40^{\circ}\text{C}$) (N=79,79,70,72,39,65,73,33,75,74) | 0 | 0 | 1 | 0 |
| Stayed Home (N=79,79,70,72,39,65,73,33,75,74) | 3 | 11 | 10 | 4 |
| Analg.Antipy Used (N=79,79,70,72,39,65,73,33,75,74) | 5 | 28 | 27 | 14 |

| End point values | Cohort 4 (3.75_Half | Cohort 4 (7.5_Full | | |
|--|------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 74 | | |
| Units: Number | | | | |
| Ecchymosis (N=79,79,71,72,39,65,73,33,75,74) | 4 | 0 | | |
| Erythema (N=79,79,71,72,39,65,73,33,75,74) | 12 | 7 | | |
| Induration (N=79,79,71,72,39,65,73,33,75,74) | 6 | 8 | | |
| Swelling (N=79,79,71,72,39,65,73,33,75,74) | 1 | 0 | | |
| Tenderness (N=0,0,0,0,0,65,73,33,75,74) | 18 | 26 | | |
| Pain (N=79,79,70,72,39,65,73,33,75,74) | 0 | 0 | | |
| Chills (N=79,79,70,72,39,0,0,0,0,0) | 0 | 0 | | |
| Malaise (N=79,79,70,72,39,0,0,0,0,0) | 0 | 0 | | |
| Myalgia (N=79,79,70,72,39,0,0,0,0,0) | 0 | 0 | | |
| Arthralgia (N=79,79,70,72,39,0,0,0,0,0) | 0 | 0 | | |
| Headache (N=79,79,70,72,39,0,0,0,0,0) | 0 | 0 | | |
| Sweating (N=79,79,70,72,39,0,0,0,0,0) | 0 | 0 | | |
| Fatigue (N=79,79,70,72,39,0,0,0,0,0) | 0 | 0 | | |
| Nausea(N=79,79,70,72,39,0,0,0,0,0) | 0 | 0 | | |
| Diarrhea (N=0,0,0,0,0,65,73,33,75,74) | 24 | 32 | | |
| Sleepiness (N=0,0,0,0,0,65,73,33,75,74) | 14 | 20 | | |
| Vomiting (N=0,0,0,0,0,65,73,33,75,74) | 17 | 18 | | |
| Irritability (N=0,0,0,0,0,65,73,33,75,74) | 14 | 13 | | |
| Chang. eating habits (N=0,0,0,0,0,65,73,33,75,74) | 18 | 25 | | |
| Unus. Crying (N=0,0,0,0,0,65,73,33,75,74) | 27 | 26 | | |
| Shivering (N=0,0,0,0,0,65,73,33,75,74) | 4 | 5 | | |
| Fever ($\geq 38^{\circ}\text{C}$) (N=79,79,70,72,39,65,73,33,75,74) | 13 | 17 | | |
| Temp ($\geq 40^{\circ}\text{C}$) (N=79,79,70,72,39,65,73,33,75,74) | 1 | 1 | | |
| Stayed Home (N=79,79,70,72,39,65,73,33,75,74) | 14 | 11 | | |
| Analg.Antipy Used (N=79,79,70,72,39,65,73,33,75,74) | 28 | 31 | | |

Statistical analyses

No statistical analyses for this end point

Primary: 5. Number of Subjects Reporting Solicited Local and Systemic Adverse Events, After Booster Vaccination

| | |
|-----------------|---|
| End point title | 5. Number of Subjects Reporting Solicited Local and Systemic Adverse Events, After Booster Vaccination ^[2] |
|-----------------|---|

End point description:

Safety was assessed as the number of subjects who reported solicited local and systemic adverse events following booster vaccination, 12 months (day 366) after the first dose of primary vaccination.

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

End point timeframe:

From day 366 through day 372.

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: No statistical analyses for this end point

| End point values | Cohort 1 (3.75_Half) | Cohort 1 (7.5_Full) | Cohort 2 (3.75_Half) | Cohort 2 (7.5_Full) |
|---|-------------------------|------------------------|-------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 24 | 30 | 35 |
| Units: Number | | | | |
| Ecchymosis | 2 | 0 | 1 | 1 |
| Erythema | 2 | 3 | 8 | 5 |
| Induration | 5 | 3 | 4 | 5 |
| Swelling | 0 | 4 | 3 | 5 |
| Inj Site Pain (N=23,24,30,35,14,0,0,0,0) | 17 | 19 | 23 | 24 |
| Tenderness (N=0,0,0,0,0,42,51,21,67,61) | 0 | 0 | 0 | 0 |
| Chills (N=23,24,30,35,14,0,0,0,0) | 1 | 1 | 3 | 5 |
| Malaise (N=23,24,30,35,14,0,0,0,0) | 5 | 3 | 8 | 11 |
| Myalgia (N=23,24,30,35,14,0,0,0,0) | 7 | 8 | 4 | 9 |
| Arthralgia (N=23,24,30,35,14,0,0,0,0) | 1 | 2 | 5 | 5 |
| Headache (N=23,24,30,35,14,0,0,0,0) | 5 | 5 | 10 | 11 |
| Sweating (N=23,24,30,35,14,0,0,0,0) | 2 | 2 | 2 | 3 |
| Fatigue (N=23,24,30,35,14,0,0,0,0) | 4 | 2 | 7 | 10 |
| Nausea (N=23,24,30,35,14,0,0,0,0) | 4 | 2 | 4 | 6 |
| Sleepiness (N=0,0,0,0,0,42,51,21,67,61) | 0 | 0 | 0 | 0 |
| Diarrhea (N=0,0,0,0,0,42,51,21,67,61) | 0 | 0 | 0 | 0 |
| Vomiting (N=0,0,0,0,0,42,51,21,67,61) | 0 | 0 | 0 | 0 |
| Irritability (N=0,0,0,0,0,42,51,21,67,61) | 0 | 0 | 0 | 0 |
| Chg. In eating habits (N=0,0,0,0,0,42,51,21,67,61) | 0 | 0 | 0 | 0 |
| Shivering (N=0,0,0,0,0,42,51,21,67,61) | 0 | 0 | 0 | 0 |
| Unus. Crying (N=0,0,0,0,0,42,51,21,67,61) | 0 | 0 | 0 | 0 |
| Fever (≥38°C) | 1 | 0 | 0 | 8 |
| Temp (≥40°C) | 0 | 0 | 0 | 0 |
| Stayed Home (N=23,24,30,35,14,41,50,21,67,61) | 3 | 2 | 3 | 10 |
| Analg.Antipy. Med. Used | 4 | 3 | 4 | 8 |

| End point values | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half) | Cohort 3 (7.5_Full) | Cohort 3 (15_No MF59) |
|---|--------------------------|-------------------------|------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 14 | 42 | 51 | 21 |
| Units: Number | | | | |
| Ecchymosis | 0 | 2 | 5 | 0 |
| Erythema | 0 | 6 | 13 | 4 |
| Induration | 0 | 4 | 7 | 3 |
| Swelling | 1 | 6 | 4 | 1 |
| Inj Site Pain (N=23,24,30,35,14,0,0,0,0) | 9 | 0 | 0 | 0 |
| Tenderness (N=0,0,0,0,0,42,51,21,67,61) | 0 | 8 | 18 | 7 |
| Chills (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | 0 | 0 |
| Malaise (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | 0 | 0 |
| Myalgia (N=23,24,30,35,14,0,0,0,0) | 4 | 0 | 0 | 0 |
| Arthralgia (N=23,24,30,35,14,0,0,0,0) | 2 | 0 | 0 | 0 |
| Headache (N=23,24,30,35,14,0,0,0,0) | 1 | 0 | 0 | 0 |
| Sweating (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | 0 | 0 |
| Fatigue (N=23,24,30,35,14,0,0,0,0) | 1 | 0 | 0 | 0 |
| Nausea (N=23,24,30,35,14,0,0,0,0) | 1 | 0 | 0 | 0 |
| Sleepiness (N=0,0,0,0,0,42,51,21,67,61) | 0 | 9 | 6 | 1 |
| Diarrhea (N=0,0,0,0,0,42,51,21,67,61) | 0 | 6 | 4 | 1 |
| Vomiting (N=0,0,0,0,0,42,51,21,67,61) | 0 | 1 | 2 | 0 |
| Irritability (N=0,0,0,0,0,42,51,21,67,61) | 0 | 5 | 3 | 3 |
| Chg. In eating habits (N=0,0,0,0,0,42,51,21,67,61) | 0 | 5 | 4 | 1 |
| Shivering (N=0,0,0,0,0,42,51,21,67,61) | 0 | 1 | 3 | 0 |
| Unus. Crying (N=0,0,0,0,0,42,51,21,67,61) | 0 | 3 | 4 | 1 |
| Fever ($\geq 38^{\circ}\text{C}$) | 0 | 6 | 15 | 2 |
| Temp ($\geq 40^{\circ}\text{C}$) | 0 | 1 | 0 | 1 |
| Stayed Home (N=23,24,30,35,14,41,50,21,67,61) | 0 | 5 | 1 | 2 |
| Analg.Antipy. Med. Used | 1 | 8 | 15 | 5 |

| End point values | Cohort 4 (3.75_Half) | Cohort 4 (7.5_Full) | | |
|-----------------------------|-------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 67 | 61 | | |
| Units: Number | | | | |
| Ecchymosis | 1 | 1 | | |
| Erythema | 5 | 9 | | |
| Induration | 5 | 4 | | |
| Swelling | 1 | 5 | | |

| | | | | |
|---|----|----|--|--|
| Inj Site Pain (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | | |
| Tenderness (N=0,0,0,0,0,42,51,21,67,61) | 11 | 19 | | |
| Chills (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | | |
| Malaise (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | | |
| Myalgia (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | | |
| Arthralgia (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | | |
| Headache (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | | |
| Sweating (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | | |
| Fatigue (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | | |
| Nausea (N=23,24,30,35,14,0,0,0,0) | 0 | 0 | | |
| Sleepiness (N=0,0,0,0,0,42,51,21,67,61) | 5 | 10 | | |
| Diarrhea (N=0,0,0,0,0,42,51,21,67,61) | 8 | 6 | | |
| Vomiting (N=0,0,0,0,0,42,51,21,67,61) | 2 | 1 | | |
| Irritability (N=0,0,0,0,0,42,51,21,67,61) | 3 | 6 | | |
| Chg. In eating habits (N=0,0,0,0,0,42,51,21,67,61) | 2 | 7 | | |
| Shivering (N=0,0,0,0,0,42,51,21,67,61) | 3 | 2 | | |
| Unus. Crying (N=0,0,0,0,0,42,51,21,67,61) | 4 | 9 | | |
| Fever ($\geq 38^{\circ}\text{C}$) | 9 | 13 | | |
| Temp ($\geq 40^{\circ}\text{C}$) | 1 | 0 | | |
| Stayed Home (N=23,24,30,35,14,41,50,21,67,61) | 5 | 5 | | |
| Analg.Antipy. Med. Used | 13 | 19 | | |

Statistical analyses

No statistical analyses for this end point

Primary: 6. Number of Subjects Reporting Solicited Local and Systemic Adverse Events, After second seasonal flu Vaccination

| | |
|-----------------|--|
| End point title | 6. Number of Subjects Reporting Solicited Local and Systemic Adverse Events, After second seasonal flu Vaccination ^[3] ^[4] |
|-----------------|--|

End point description:

Safety was assessed as the number of subjects who reported solicited local and systemic adverse events. For subjects aged <9 years of age at the time of booster received a second seasonal flu dose on day 387 for influenza vaccine naive subjects.

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

End point timeframe:

Day 387 through day 394

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: No statistical analyses for this end point

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point

| End point values | Cohort 2 (3.75_Half | Cohort 2 (7.5_Full | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half |
|---|------------------------|-----------------------|--------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 22 | 26 | 11 | 36 |
| Units: Number | | | | |
| Injection Site Ecchymosis | 0 | 1 | 0 | 0 |
| Injection Site Erythema | 4 | 6 | 0 | 10 |
| Injection Site Induration | 4 | 7 | 0 | 8 |
| Injection Site Swelling | 4 | 5 | 1 | 7 |
| Injection Site Pain (N=22,26,11,0,0,0,0,0) | 13 | 13 | 7 | 0 |
| Tenderness (N=0,0,0,36,45,17,63,60) | 0 | 0 | 0 | 8 |
| Chills (N=22,26,11,0,0,0,0,0) | 0 | 1 | 0 | 0 |
| Malaise (N=22,26,11,0,0,0,0,0) | 1 | 2 | 1 | 0 |
| Myalgia (N=22,26,11,0,0,0,0,0) | 1 | 2 | 1 | 0 |
| Arthralgia (N=22,26,11,0,0,0,0,0) | 1 | 2 | 1 | 0 |
| Headache (N=22,26,11,0,0,0,0,0) | 3 | 3 | 1 | 0 |
| Sweating (N=22,26,11,0,0,0,0,0) | 0 | 1 | 0 | 0 |
| Fatigue (N=22,26,11,0,0,0,0,0) | 3 | 6 | 2 | 0 |
| Nausea (N=22,26,11,0,0,0,0,0) | 1 | 2 | 1 | 0 |
| Sleepiness (N=0,0,0,36,45,17,63,60) | 0 | 0 | 0 | 1 |
| Diarrhoea (N=0,0,0,36,45,17,63,60) | 0 | 0 | 0 | 3 |
| Vomiting (N=0,0,0,36,45,17,63,60) | 0 | 0 | 0 | 1 |
| Irritability (N=0,0,0,36,45,17,63,60) | 0 | 0 | 0 | 2 |
| Chg. In eating habits (N=0,0,0,36,45,17,63,60) | 0 | 0 | 0 | 3 |
| Shivering (N=0,0,0,36,45,17,63,60) | 0 | 0 | 0 | 1 |
| Unus. Crying (N=0,0,0,36,45,17,63,60) | 0 | 0 | 0 | 1 |
| Fever ($\geq 38^{\circ}\text{C}$) | 1 | 2 | 1 | 3 |
| Temp ($\geq 40^{\circ}\text{C}$) | 0 | 0 | 0 | 0 |
| Stayed Home | 1 | 0 | 0 | 1 |
| Analg.Antipy. Med. Used | 2 | 6 | 1 | 3 |

| End point values | Cohort 3 (7.5_Full | Cohort 3 (15_No MF59) | Cohort 4 (3.75_Half | Cohort 4 (7.5_Full |
|---|-----------------------|--------------------------|------------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 45 | 17 | 63 | 60 |
| Units: Number | | | | |
| Injection Site Ecchymosis | 1 | 1 | 1 | 1 |
| Injection Site Erythema | 10 | 2 | 6 | 6 |
| Injection Site Induration | 8 | 3 | 6 | 5 |
| Injection Site Swelling | 7 | 2 | 3 | 3 |
| Injection Site Pain (N=22,26,11,0,0,0,0,0) | 0 | 0 | 0 | 0 |
| Tenderness (N=0,0,0,36,45,17,63,60) | 11 | 4 | 14 | 13 |
| Chills (N=22,26,11,0,0,0,0,0) | 0 | 0 | 0 | 0 |
| Malaise (N=22,26,11,0,0,0,0,0) | 0 | 0 | 0 | 0 |
| Myalgia (N=22,26,11,0,0,0,0,0) | 0 | 0 | 0 | 0 |
| Arthralgia (N=22,26,11,0,0,0,0,0) | 0 | 0 | 0 | 0 |
| Headache (N=22,26,11,0,0,0,0,0) | 0 | 0 | 0 | 0 |
| Sweating (N=22,26,11,0,0,0,0,0) | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|----|----|
| Fatigue (N=22,26,11,0,0,0,0) | 0 | 0 | 0 | 0 |
| Nausea (N=22,26,11,0,0,0,0) | 0 | 0 | 0 | 0 |
| Sleepiness (N=0,0,0,36,45,17,63,60) | 1 | 1 | 3 | 5 |
| Diarrhoea (N=0,0,0,36,45,17,63,60) | 3 | 0 | 7 | 7 |
| Vomiting (N=0,0,0,36,45,17,63,60) | 1 | 0 | 5 | 2 |
| Irritability (N=0,0,0,36,45,17,63,60) | 3 | 3 | 4 | 2 |
| Chg. In eating habits (N=0,0,0,36,45,17,63,60) | 2 | 1 | 6 | 5 |
| Shivering (N=0,0,0,36,45,17,63,60) | 0 | 0 | 2 | 1 |
| Unus. Crying (N=0,0,0,36,45,17,63,60) | 3 | 1 | 8 | 3 |
| Fever ($\geq 38^{\circ}\text{C}$) | 4 | 0 | 7 | 10 |
| Temp ($\geq 40^{\circ}\text{C}$) | 0 | 0 | 0 | 0 |
| Stayed Home | 0 | 0 | 2 | 3 |
| Analg.Antipy. Med. Used | 6 | 1 | 10 | 11 |

Statistical analyses

No statistical analyses for this end point

Primary: 7. Number of Subjects Reporting Unsolicited Adverse Events after primary and booster vaccination.

| | |
|-----------------|--|
| End point title | 7. Number of Subjects Reporting Unsolicited Adverse Events after primary and booster vaccination. ^[5] |
|-----------------|--|

End point description:

Safety was assessed as the number of subjects who reported unsolicited adverse events after primary vaccination and following booster vaccination, 12 months (day 366) after the first dose of primary vaccination. For influenza vaccine naive subjects aged <9 years of age at the time of booster received a second seasonal flu dose on day 387.

All AEs were collected from day 1 to day 43 after primary vaccination, from day 366 through day 387 after booster vaccination and day 387 to day 401 for subjects who receive second seasonal flu dose

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

End point timeframe:

Day 1 through day 43, day 366 through day 387, day 387 through day 401.

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: No statistical analyses for this end point.

| End point values | Cohort 1 (3.75_Half) | Cohort 1 (7.5_Full) | Cohort 2 (3.75_Half) | Cohort 2 (7.5_Full) |
|--|-------------------------|------------------------|-------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 79 | 79 | 71 | 72 |
| Units: Number | | | | |
| Any AE-Primary vacc.;79,79,71,72,39,65,73,33,75,74 | 28 | 26 | 31 | 31 |
| Possibly related AEs- 79,79,71,72,39,65,73,33,75,74 | 15 | 18 | 15 | 18 |
| Any AE-booster vacc.;74,78,80,80,37,65,74,30,75,73 | 3 | 4 | 6 | 6 |
| Possibly related AEs- 74,78,80,80,37,65,74,30,75,73 | 2 | 1 | 2 | 3 |
| Any AE-2nd seasonal;0,0,30,35,14,41,50,21,66,60 | 0 | 0 | 1 | 5 |

| | | | | |
|--|---|---|---|---|
| Possibly related AEs- 0,0,30,35,14,41,50,21,66,60 | 0 | 0 | 0 | 0 |
|--|---|---|---|---|

| End point values | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half) | Cohort 3 (7.5_Full) | Cohort 3 (15_No MF59) |
|--|--------------------------|-------------------------|------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 39 | 65 | 71 | 33 |
| Units: Number | | | | |
| Any AE-Primary vacc.;79,79,71,72,39,65,73,33,75,74 | 17 | 33 | 32 | 23 |
| Possibly related AEs- 79,79,71,72,39,65,73,33,75,74 | 11 | 4 | 9 | 7 |
| Any AE-booster vacc.;74,78,80,80,37,65,74,30,75,73 | 1 | 5 | 10 | 2 |
| Possibly related AEs- 74,78,80,80,37,65,74,30,75,73 | 0 | 1 | 4 | 1 |
| Any AE-2nd seasonal;0,0,30,35,14,41,50,21,66,60 | 1 | 1 | 8 | 2 |
| Possibly related AEs- 0,0,30,35,14,41,50,21,66,60 | 0 | 0 | 2 | 0 |

| End point values | Cohort 4 (3.75_Half) | Cohort 4 (7.5_Full) | | |
|--|-------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 74 | | |
| Units: Number | | | | |
| Any AE-Primary vacc.;79,79,71,72,39,65,73,33,75,74 | 51 | 50 | | |
| Possibly related AEs- 79,79,71,72,39,65,73,33,75,74 | 20 | 22 | | |
| Any AE-booster vacc.;74,78,80,80,37,65,74,30,75,73 | 20 | 16 | | |
| Possibly related AEs- 74,78,80,80,37,65,74,30,75,73 | 6 | 4 | | |
| Any AE-2nd seasonal;0,0,30,35,14,41,50,21,66,60 | 14 | 17 | | |
| Possibly related AEs- 0,0,30,35,14,41,50,21,66,60 | 3 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Primary: 8. Number of Subjects Reporting Unsolicited Adverse Events.

| | |
|-----------------|--|
| End point title | 8. Number of Subjects Reporting Unsolicited Adverse Events. ^[6] |
|-----------------|--|

End point description:

Safety was assessed as the number of subjects who reported unsolicited adverse events.

SAEs, new onset of chronic diseases, AEs leading to withdrawal from the study were collected from day 1 to day 546 following 2-dose vaccination H1N1sw monovalent vaccine

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: | |
| SAEs, NOCDs, AEs leading to withdrawal-day 1 to day 546 | |
| Notes: | |
| [6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. | |
| Justification: No statistical analyses for this end point. | |

| End point values | Cohort 1 (3.75_Half) | Cohort 1 (7.5_Full) | Cohort 2 (3.75_Half) | Cohort 2 (7.5_Full) |
|--------------------------------|-------------------------|------------------------|-------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 80 | 79 | 72 | 73 |
| Units: Number | | | | |
| Any SAEs | 3 | 2 | 1 | 3 |
| At least possibly related SAEs | 0 | 1 | 0 | 0 |
| AEs leading to discontinuation | 2 | 0 | 0 | 1 |
| New onset of chronic disease | 0 | 3 | 0 | 0 |

| End point values | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half) | Cohort 3 (7.5_Full) | Cohort 3 (15_No MF59) |
|--------------------------------|--------------------------|-------------------------|------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 39 | 65 | 71 | 34 |
| Units: Number | | | | |
| Any SAEs | 0 | 7 | 8 | 5 |
| At least possibly related SAEs | 0 | 0 | 1 | 0 |
| AEs leading to discontinuation | 1 | 1 | 0 | 1 |
| New onset of chronic disease | 0 | 0 | 0 | 1 |

| End point values | Cohort 4 (3.75_Half) | Cohort 4 (7.5_Full) | | |
|--------------------------------|-------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 76 | | |
| Units: Number | | | | |
| Any SAEs | 11 | 8 | | |
| At least possibly related SAEs | 1 | 0 | | |
| AEs leading to discontinuation | 1 | 1 | | |
| New onset of chronic disease | 1 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Percentages of subjects achieving seroconversion against A/H1N1 Strain following a booster dose as measured by hemagglutination inhibition (HI) assay.

| | |
|--|---|
| End point title | 9. Percentages of subjects achieving seroconversion against A/H1N1 Strain following a booster dose as measured by hemagglutination inhibition (HI) assay. |
| End point description: | |
| Immunogenicity was measured in terms of percentage of subjects achieving seroconversion or significant increase in HI titer against the A/H1N1 strain, after a booster dose with aTIV, administered 12 months after primary vaccination according to CHMP criterion. | |
| At least one CHMP criterion as assessed three weeks after the booster dose should be met within each age cohort to fulfill regulatory requirements. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 387 (3 weeks post booster vaccination) | |

| End point values | Cohort 1 (3.75_Half) | Cohort 1 (7.5_Full) | Cohort 2 (3.75_Half) | Cohort 2 (7.5_Full) |
|----------------------------------|-------------------------|------------------------|-------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 19 | 20 | 20 | 29 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 387 (From Day 366) | 89 (67 to 99) | 80 (56 to 94) | 95 (75 to 100) | 100 (88 to 100) |

| End point values | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half) | Cohort 3 (7.5_Full) | Cohort 3 (15_No MF59) |
|----------------------------------|--------------------------|-------------------------|------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 32 | 38 | 17 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 387 (From Day 366) | 100 (69 to 100) | 94 (79 to 99) | 95 (82 to 99) | 100 (80 to 100) |

| End point values | Cohort 4 (3.75_Half) | Cohort 4 (7.5_Full) | | |
|----------------------------------|-------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 40 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 387 (From Day 366) | 85 (72 to 94) | 90 (76 to 97) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Percentages of subjects achieving HI titers $\geq 1:40$ against A/H1N1 Strain following a booster dose

| | |
|-----------------|--|
| End point title | 10. Percentages of subjects achieving HI titers $\geq 1:40$ against A/H1N1 Strain following a booster dose |
|-----------------|--|

End point description:

Immunogenicity was measured in terms of percentage of subjects achieving HI titers $\geq 1:40$ against A/H1N1 strain after a booster dose with aTIV, administered 12 months after primary vaccination according to CHMP criterion.

At least one CHMP criterion as assessed three weeks after the booster dose should be met within each age cohort to fulfill regulatory requirements.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 366 and Day 387 (3 weeks post second vaccination)

| End point values | Cohort 1 (3.75_Half) | Cohort 1 (7.5_Full) | Cohort 2 (3.75_Half) | Cohort 2 (7.5_Full) |
|--|-------------------------|------------------------|-------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 22 | 24 | 31 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 366 | 86 (64 to 97) | 95 (77 to 100) | 100 (86 to 100) | 100 (89 to 100) |
| Day 387 (N=19,20,20,29,10,32,38,17,47,40) | 100 (82 to 100) | 100 (83 to 100) | 100 (83 to 100) | 100 (88 to 100) |

| End point values | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half) | Cohort 3 (7.5_Full) | Cohort 3 (15_No MF59) |
|--|--------------------------|-------------------------|------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 39 | 46 | 21 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 366 | 91 (59 to 100) | 100 (91 to 100) | 100 (92 to 100) | 71 (48 to 89) |
| Day 387 (N=19,20,20,29,10,32,38,17,47,40) | 100 (69 to 100) | 100 (89 to 100) | 100 (91 to 100) | 100 (80 to 100) |

| End point values | Cohort 4 (3.75_Half) | Cohort 4 (7.5_Full) | | |
|--|-------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 54 | 47 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Day 366 | 94 (85 to 99) | 100 (92 to 100) | | |
| Day 387 (N=19,20,20,29,10,32,38,17,47,40) | 100 (92 to 100) | 100 (91 to 100) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 11. Geometric mean Ratios against A/H1N1 strain following a booster dose as determined by HI assay

| | |
|-----------------|--|
| End point title | 11. Geometric mean Ratios against A/H1N1 strain following a booster dose as determined by HI assay |
|-----------------|--|

End point description:

Immunogenicity was measured in terms of geometric mean ratios. The ratio of postvaccination to prevaccination HI GMTs after a booster dose with aTIV, administered 12 months after primary vaccination according to CHMP criterion was assessed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 366 and Day 387 (3 weeks post booster vaccination)

| End point values | Cohort 1 (3.75_Half) | Cohort 1 (7.5_Full) | Cohort 2 (3.75_Half) | Cohort 2 (7.5_Full) |
|--|-------------------------|------------------------|-------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 19 | 20 | 20 | 29 |
| Units: Ratios | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 387/Day 366 | 15 (6.89 to 33) | 8.47 (4.34 to 17) | 28 (15 to 51) | 26 (16 to 43) |

| End point values | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half) | Cohort 3 (7.5_Full) | Cohort 3 (15_No MF59) |
|--|--------------------------|-------------------------|------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 32 | 38 | 17 |
| Units: Ratios | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 387/Day 366 | 30 (14 to 62) | 19 (9.73 to 39) | 17 (8.88 to 31) | 36 (16 to 81) |

| End point values | Cohort 4 (3.75_Half) | Cohort 4 (7.5_Full) | | |
|-----------------------------|-------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 40 | | |
| Units: Ratios | | | | |

| | | | | |
|--|---------------|---------------|--|--|
| geometric mean (confidence interval 95%) | | | | |
| Day 387/Day 366 | 33 (17 to 63) | 23 (11 to 46) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 12. Geometric mean titers against A/H1N1 strain as determined by HI assay in pooled population

| | |
|--|--|
| End point title | 12. Geometric mean titers against A/H1N1 strain as determined by HI assay in pooled population |
| End point description: Immunogenicity was measured in terms of geometric mean titers against A/H1N1 strain, 3 weeks after second vaccination in pooled children population. | |
| End point type | Secondary |
| End point timeframe: Day 1 and Day 43 (3 weeks post second vaccination) | |

| End point values | All Cohorts (7.5_Full MF59) | All Cohorts (3.75_Half MF59) | | |
|--|-----------------------------|------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 238 | 239 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 1 | 7.55 (6.03 to 9.45) | 7.75 (6.16 to 9.75) | | |
| Day 43 | 756 (633 to 902) | 539 (449 to 646) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Difference in HI GMTs of half and full dose MF59 |
| Statistical analysis description: To demonstrate the non-inferiority of immune response in terms of GMTs in subjects receiving 3.75 HA and half MF59, versus subjects receiving 7.5 HA and full MF59, 3 weeks after second vaccination. | |
| Comparison groups | All Cohorts (7.5_Full MF59) v All Cohorts (3.75_Half MF59) |
| Number of subjects included in analysis | 477 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[7] |
| Method | ANOVA |
| Parameter estimate | Vaccine group difference |
| Point estimate | 0.72 |

| Confidence interval | |
|---------------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.6 |
| upper limit | 0.85 |

Notes:

[7] - Non-inferiority will be concluded if the lower limit of the two sided 95% CI for the between group difference (3.75_Half MF59-7.5_Full MF59) in terms of post-immunization GMTs (at day 43) is higher or equal to 0.5.

If the hypothesis above can be rejected the same non-inferiority hypothesis were to be tested using a non-inferiority margin of 0.67.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to Day 546

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 14.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | Cohort 1 (3.75_Half MF59) |
|-----------------------|---------------------------|

Reporting group description:

Subjects aged ≥ 9 to ≤ 17 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an adjuvanted trivalent influenza vaccine (aTIV).

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 1 (7.5_Full MF59) |
|-----------------------|--------------------------|

Reporting group description:

Subjects aged ≥ 9 to ≤ 17 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|-----------------------|---------------------------|
| Reporting group title | Cohort 2 (3.75_Half MF59) |
|-----------------------|---------------------------|

Reporting group description:

Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 2 (7.5_Full MF59) |
|-----------------------|--------------------------|

Reporting group description:

Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|-----------------------|-----------------------|
| Reporting group title | Cohort 2 (15_No MF59) |
|-----------------------|-----------------------|

Reporting group description:

Subjects aged ≥ 3 to ≤ 8 years received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|-----------------------|---------------------------|
| Reporting group title | Cohort 3 (3.75_Half MF59) |
|-----------------------|---------------------------|

Reporting group description:

Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 3 (7.5_Full MF59) |
|-----------------------|--------------------------|

Reporting group description:

Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|-----------------------|-----------------------|
| Reporting group title | Cohort 3 (15_No MF59) |
|-----------------------|-----------------------|

Reporting group description:

Subjects aged ≥ 12 to ≤ 35 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|-----------------------|---------------------------|
| Reporting group title | Cohort 4 (3.75_Half MF59) |
|-----------------------|---------------------------|

Reporting group description:

Subjects aged ≥ 6 to ≤ 11 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| | |
|-----------------------|--------------------------|
| Reporting group title | Cohort 4 (7.5_Full MF59) |
|-----------------------|--------------------------|

Reporting group description:

Subjects aged ≥ 6 to ≤ 11 months received 2 doses of H1N1 vaccine administered 3 weeks apart, followed by a booster dose 12 months after first vaccination with an aTIV.

| Serious adverse events | Cohort 1 (3.75_Half MF59) | Cohort 1 (7.5_Full MF59) | Cohort 2 (3.75_Half MF59) |
|---|---------------------------|--------------------------|---------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 79 (3.80%) | 2 / 79 (2.53%) | 1 / 71 (1.41%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Joint Dislocation | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxicity to various agents | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Concussion | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 1 / 71 (1.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skull fracture | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 1 / 71 (1.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Accidental exposure | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chemical poisoning | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Convulsion | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 79 (0.00%) | 1 / 79 (1.27%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 1 / 79 (1.27%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 1 / 79 (1.27%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Respiratory, thoracic and mediastinal disorders | | | |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchospasm | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute tonsillitis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Amoebic dysentery | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Giardiasis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory syncytial virus bronchiolitis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Cohort 2 (7.5_Full MF59) | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half MF59) |
|---|--------------------------|-----------------------|---------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 72 (4.17%) | 0 / 39 (0.00%) | 7 / 65 (10.77%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Joint Dislocation | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Concussion | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skull fracture | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Accidental exposure | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chemical poisoning | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Convulsion | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Migraine | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchospasm | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 72 (1.39%) | 0 / 39 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 72 (2.78%) | 0 / 39 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Acute tonsillitis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Amoebic dysentery | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Giardiasis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchiolitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory syncytial virus bronchiolitis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Cohort 3 (7.5_Full MF59) | Cohort 3 (15_No MF59) | Cohort 4 (3.75_Half MF59) |
|---|--------------------------|-----------------------|---------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 73 (10.96%) | 5 / 33 (15.15%) | 11 / 75 (14.67%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Joint Dislocation | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Concussion | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skull fracture | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Accidental exposure | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chemical poisoning | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Convulsion | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 1 / 75 (1.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |

| | | | |
|---|----------------|----------------|----------------|
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 1 / 75 (1.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 33 (0.00%) | 2 / 75 (2.67%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchospasm | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 33 (3.03%) | 4 / 75 (5.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 33 (3.03%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute tonsillitis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Amoebic dysentery | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 33 (3.03%) | 3 / 75 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Dengue fever | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 1 / 75 (1.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Giardiasis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 33 (3.03%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 33 (3.03%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 33 (3.03%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 33 (3.03%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 1 / 75 (1.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 1 / 75 (1.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory syncytial virus bronchiolitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 1 / 75 (1.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|--------------------------|--|--|
| Serious adverse events | Cohort 4 (7.5_Full MF59) | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 74 (10.81%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Joint Dislocation | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Concussion | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skull fracture | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Accidental exposure | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chemical poisoning | | | |
| subjects affected / exposed | 1 / 74 (1.35%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Convulsion | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 74 (1.35%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchospasm | | | |
| subjects affected / exposed | 1 / 74 (1.35%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 74 (1.35%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 74 (5.41%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute tonsillitis | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Amoebic dysentery | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Giardiasis | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Laryngitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory syncytial virus bronchiolitis | | | |
| subjects affected / exposed | 2 / 74 (2.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Cohort 1 (3.75_Half MF59) | Cohort 1 (7.5_Full MF59) | Cohort 2 (3.75_Half MF59) |
|---|----------------------------------|---------------------------------|----------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 71 / 79 (89.87%) | 72 / 79 (91.14%) | 63 / 71 (88.73%) |
| Nervous system disorders | | | |
| Headache | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 28 / 79 (35.44%) | 29 / 79 (36.71%) | 17 / 71 (23.94%) |
| occurrences (all) | 42 | 47 | 24 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Chills | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 79 (3.80%) | 10 / 79 (12.66%) | 6 / 71 (8.45%) |
| occurrences (all) | 4 | 12 | 7 |
| Crying | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | 0 / 79 (0.00%) | 0 / 71 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 25 / 79 (31.65%) | 28 / 79 (35.44%) | 26 / 71 (36.62%) |
| occurrences (all) | 35 | 40 | 38 |
| Injection site erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 12 / 79 (15.19%) | 18 / 79 (22.78%) | 24 / 71 (33.80%) |
| occurrences (all) | 12 | 20 | 30 |
| Injection site haemorrhage | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 6 / 79 (7.59%) | 7 / 79 (8.86%) | 10 / 71 (14.08%) |
| occurrences (all) | 10 | 9 | 13 |
| Injection site induration | | | |

| | | | |
|---|-------------------------|-------------------------|------------------------|
| alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 18 / 79 (22.78%) 21 | 17 / 79 (21.52%) 20 | 15 / 71 (21.13%) 18 |
| Injection site pain alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 62 / 79 (78.48%) 115 | 67 / 79 (84.81%) 131 | 49 / 71 (69.01%) 96 |
| Injection site swelling alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 9 / 79 (11.39%) 9 | 17 / 79 (21.52%) 21 | 15 / 71 (21.13%) 17 |
| Malaise alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 14 / 79 (17.72%) 17 | 20 / 79 (25.32%) 27 | 20 / 71 (28.17%) 23 |
| Pyrexia alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 5 | 1 / 79 (1.27%) 1 | 19 / 71 (26.76%) 26 |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 3 / 79 (3.80%) 3 | 1 / 79 (1.27%) 2 | 3 / 71 (4.23%) 5 |
| Diarrhoea alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 7 / 79 (8.86%) 8 | 1 / 79 (1.27%) 1 | 5 / 71 (7.04%) 6 |
| Nausea alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 13 / 79 (16.46%) 14 | 10 / 79 (12.66%) 11 | 10 / 71 (14.08%) 10 |
| Vomiting alternative assessment type: Systematic | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | 0 / 79 (0.00%) 0 | 2 / 71 (2.82%) 3 |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) | 3 / 79 (3.80%) 3 | 2 / 79 (2.53%) 2 | 4 / 71 (5.63%) 4 |
| Skin and subcutaneous tissue disorders Ecchymosis subjects affected / exposed occurrences (all) Hyperhidrosis subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 6 / 79 (7.59%) 9 | 1 / 79 (1.27%) 1 5 / 79 (6.33%) 7 | 0 / 71 (0.00%) 0 3 / 71 (4.23%) 3 |
| Psychiatric disorders Eating disorder subjects affected / exposed occurrences (all) Irritability alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 0 / 79 (0.00%) 0 | 0 / 79 (0.00%) 0 0 / 79 (0.00%) 0 | 1 / 71 (1.41%) 1 1 / 71 (1.41%) 1 |
| Musculoskeletal and connective tissue disorders Arthralgia alternative assessment type: Systematic subjects affected / exposed occurrences (all) Myalgia alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 13 / 79 (16.46%) 13 28 / 79 (35.44%) 32 | 12 / 79 (15.19%) 15 28 / 79 (35.44%) 32 | 10 / 71 (14.08%) 13 10 / 71 (14.08%) 12 |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Conjunctivitis | 2 / 79 (2.53%) 2 | 0 / 79 (0.00%) 0 | 1 / 71 (1.41%) 1 |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 0 / 79 (0.00%) 0 | 0 / 71 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 2 | 3 / 79 (3.80%) 4 | 3 / 71 (4.23%) 3 |
| Rhinitis subjects affected / exposed occurrences (all) | 6 / 79 (7.59%) 6 | 6 / 79 (7.59%) 7 | 5 / 71 (7.04%) 5 |
| Tonsillitis subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | 0 / 79 (0.00%) 0 | 1 / 71 (1.41%) 1 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 4 | 1 / 79 (1.27%) 1 | 5 / 71 (7.04%) 5 |

| Non-serious adverse events | Cohort 2 (7.5_Full MF59) | Cohort 2 (15_No MF59) | Cohort 3 (3.75_Half MF59) |
|---|-----------------------------|--------------------------|------------------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 66 / 72 (91.67%) | 34 / 39 (87.18%) | 61 / 65 (93.85%) |
| Nervous system disorders Headache alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 17 / 72 (23.61%) 24 | 9 / 39 (23.08%) 11 | 0 / 65 (0.00%) 0 |
| Somnolence subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 39 (0.00%) 0 | 21 / 65 (32.31%) 41 |
| General disorders and administration site conditions Chills alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 11 / 72 (15.28%) 13 | 2 / 39 (5.13%) 2 | 7 / 65 (10.77%) 10 |
| Crying alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 39 (0.00%) 0 | 21 / 65 (32.31%) 34 |
| Fatigue | | | |

| | | | |
|--|------------------|------------------|------------------|
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 24 / 72 (33.33%) | 10 / 39 (25.64%) | 0 / 65 (0.00%) |
| occurrences (all) | 46 | 19 | 0 |
| Injection site erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 28 / 72 (38.89%) | 8 / 39 (20.51%) | 22 / 65 (33.85%) |
| occurrences (all) | 40 | 10 | 33 |
| Injection site haemorrhage | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 11 / 72 (15.28%) | 10 / 39 (25.64%) | 6 / 65 (9.23%) |
| occurrences (all) | 13 | 13 | 6 |
| Injection site induration | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 21 / 72 (29.17%) | 6 / 39 (15.38%) | 17 / 65 (26.15%) |
| occurrences (all) | 34 | 6 | 22 |
| Injection site pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 49 / 72 (68.06%) | 23 / 39 (58.97%) | 22 / 65 (33.85%) |
| occurrences (all) | 103 | 42 | 32 |
| Injection site swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 19 / 72 (26.39%) | 5 / 39 (12.82%) | 13 / 65 (20.00%) |
| occurrences (all) | 22 | 6 | 16 |
| Malaise | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 15 / 72 (20.83%) | 8 / 39 (20.51%) | 0 / 65 (0.00%) |
| occurrences (all) | 21 | 16 | 0 |
| Pyrexia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 24 / 72 (33.33%) | 6 / 39 (15.38%) | 37 / 65 (56.92%) |
| occurrences (all) | 48 | 7 | 60 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |

| | | | |
|---|------------------|-----------------|------------------|
| subjects affected / exposed | 2 / 72 (2.78%) | 3 / 39 (7.69%) | 0 / 65 (0.00%) |
| occurrences (all) | 2 | 5 | 0 |
| Diarrhoea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 6 / 72 (8.33%) | 3 / 39 (7.69%) | 24 / 65 (36.92%) |
| occurrences (all) | 8 | 5 | 41 |
| Nausea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 10 / 72 (13.89%) | 4 / 39 (10.26%) | 0 / 65 (0.00%) |
| occurrences (all) | 15 | 8 | 0 |
| Vomiting | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 72 (6.94%) | 2 / 39 (5.13%) | 12 / 65 (18.46%) |
| occurrences (all) | 27 | 2 | 19 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 72 (2.78%) | 3 / 39 (7.69%) | 0 / 65 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 2 / 39 (5.13%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 4 / 72 (5.56%) | 0 / 39 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Psychiatric disorders | | | |
| Eating disorder | | | |
| subjects affected / exposed | 2 / 72 (2.78%) | 0 / 39 (0.00%) | 23 / 65 (35.38%) |
| occurrences (all) | 2 | 0 | 36 |
| Irritability | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 72 (5.56%) | 2 / 39 (5.13%) | 21 / 65 (32.31%) |
| occurrences (all) | 5 | 2 | 37 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|--|------------------------|-----------------------|------------------------|
| Arthralgia alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 11 / 72 (15.28%) 14 | 4 / 39 (10.26%) 5 | 0 / 65 (0.00%) 0 |
| Myalgia alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 20 / 72 (27.78%) 26 | 7 / 39 (17.95%) 10 | 0 / 65 (0.00%) 0 |
| Infections and infestations | | | |
| Bronchitis subjects affected / exposed occurrences (all) | 1 / 72 (1.39%) 1 | 0 / 39 (0.00%) 0 | 0 / 65 (0.00%) 0 |
| Conjunctivitis subjects affected / exposed occurrences (all) | 2 / 72 (2.78%) 2 | 0 / 39 (0.00%) 0 | 1 / 65 (1.54%) 1 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 2 / 72 (2.78%) 4 | 1 / 39 (2.56%) 1 | 15 / 65 (23.08%) 20 |
| Rhinitis subjects affected / exposed occurrences (all) | 7 / 72 (9.72%) 9 | 1 / 39 (2.56%) 1 | 4 / 65 (6.15%) 4 |
| Tonsillitis subjects affected / exposed occurrences (all) | 1 / 72 (1.39%) 2 | 0 / 39 (0.00%) 0 | 3 / 65 (4.62%) 3 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 3 / 72 (4.17%) 4 | 3 / 39 (7.69%) 3 | 1 / 65 (1.54%) 1 |

| Non-serious adverse events | Cohort 3 (7.5_Full MF59) | Cohort 3 (15_No MF59) | Cohort 4 (3.75_Half MF59) |
|--|-----------------------------|--------------------------|------------------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 65 / 73 (89.04%) | 28 / 33 (84.85%) | 70 / 75 (93.33%) |
| Nervous system disorders | | | |
| Headache alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 75 (0.00%) 0 |

| | | | |
|--|------------------|------------------|------------------|
| Somnolence | | | |
| subjects affected / exposed | 35 / 73 (47.95%) | 9 / 33 (27.27%) | 17 / 75 (22.67%) |
| occurrences (all) | 49 | 13 | 33 |
| General disorders and administration site conditions | | | |
| Chills | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 10 / 73 (13.70%) | 2 / 33 (6.06%) | 5 / 75 (6.67%) |
| occurrences (all) | 10 | 2 | 10 |
| Crying | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 29 / 73 (39.73%) | 10 / 33 (30.30%) | 32 / 75 (42.67%) |
| occurrences (all) | 47 | 13 | 54 |
| Fatigue | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 30 / 73 (41.10%) | 10 / 33 (30.30%) | 16 / 75 (21.33%) |
| occurrences (all) | 53 | 16 | 26 |
| Injection site haemorrhage | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 15 / 73 (20.55%) | 6 / 33 (18.18%) | 6 / 75 (8.00%) |
| occurrences (all) | 20 | 8 | 9 |
| Injection site induration | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 23 / 73 (31.51%) | 8 / 33 (24.24%) | 10 / 75 (13.33%) |
| occurrences (all) | 32 | 11 | 18 |
| Injection site pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 44 / 73 (60.27%) | 17 / 33 (51.52%) | 29 / 75 (38.67%) |
| occurrences (all) | 90 | 32 | 50 |
| Injection site swelling | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 16 / 73 (21.92%) | 5 / 33 (15.15%) | 3 / 75 (4.00%) |
| occurrences (all) | 20 | 6 | 42 |
| Malaise | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 38 / 73 (52.05%) | 12 / 33 (36.36%) | 32 / 75 (42.67%) |
| occurrences (all) | 63 | 19 | 42 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 1 / 33 (3.03%) | 0 / 75 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 30 / 73 (41.10%) | 10 / 33 (30.30%) | 35 / 75 (46.67%) |
| occurrences (all) | 43 | 15 | 68 |
| Nausea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 25 / 73 (34.25%) | 4 / 33 (12.12%) | 21 / 75 (28.00%) |
| occurrences (all) | 27 | 6 | 33 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 1 / 75 (1.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 73 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 75 (0.00%) 0 |
| Psychiatric disorders | | | |
| Eating disorder | | | |
| subjects affected / exposed | 33 / 73 (45.21%) | 8 / 33 (24.24%) | 24 / 75 (32.00%) |
| occurrences (all) | 42 | 14 | 37 |
| Irritability | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 21 / 73 (28.77%) | 7 / 33 (21.21%) | 15 / 75 (20.00%) |
| occurrences (all) | 35 | 13 | 26 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 73 (0.00%) | 0 / 33 (0.00%) | 0 / 75 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 3 / 33 (9.09%) | 2 / 75 (2.67%) |
| occurrences (all) | 2 | 4 | 2 |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | 1 / 33 (3.03%) | 2 / 75 (2.67%) |
| occurrences (all) | 1 | 1 | 3 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 16 / 73 (21.92%) | 13 / 33 (39.39%) | 40 / 75 (53.33%) |
| occurrences (all) | 18 | 14 | 64 |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | 1 / 33 (3.03%) | 1 / 75 (1.33%) |
| occurrences (all) | 2 | 1 | 1 |
| Tonsillitis | | | |
| subjects affected / exposed | 5 / 73 (6.85%) | 0 / 33 (0.00%) | 6 / 75 (8.00%) |
| occurrences (all) | 6 | 0 | 6 |
| Upper respiratory tract infection | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 4 / 73 (5.48%) | 0 / 33 (0.00%) | 1 / 75 (1.33%) |
| occurrences (all) | 4 | 0 | 1 |

| | | | |
|---|--------------------------|--|--|
| Non-serious adverse events | Cohort 4 (7.5_Full MF59) | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 69 / 74 (93.24%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences (all) | 0 | | |
| Somnolence | | | |
| subjects affected / exposed | 28 / 74 (37.84%) | | |
| occurrences (all) | 48 | | |
| General disorders and administration site conditions | | | |
| Chills | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 6 / 74 (8.11%) | | |
| occurrences (all) | 9 | | |
| Crying | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 31 / 74 (41.89%) | | |
| occurrences (all) | 52 | | |
| Fatigue | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site erythema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 16 / 74 (21.62%) | | |
| occurrences (all) | 24 | | |
| Injection site haemorrhage | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 74 (1.35%) | | |
| occurrences (all) | 2 | | |

| | | | |
|---|------------------------|--|--|
| Injection site induration alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 12 / 74 (16.22%) 19 | | |
| Injection site pain alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 34 / 74 (45.95%) 69 | | |
| Injection site swelling alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 6 / 74 (8.11%) 8 | | |
| Malaise alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 74 (0.00%) 0 | | |
| Pyrexia alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 39 / 74 (52.70%) 66 | | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 1 / 74 (1.35%) 1 | | |
| Diarrhoea alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 38 / 74 (51.35%) 84 | | |
| Nausea alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 74 (0.00%) 0 | | |
| Vomiting alternative assessment type: Systematic | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 22 / 74 (29.73%) 31 | | |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 74 (0.00%) 0 | | |
| Skin and subcutaneous tissue disorders Ecchymosis subjects affected / exposed occurrences (all) Hyperhidrosis subjects affected / exposed occurrences (all) | 0 / 74 (0.00%) 0 0 / 74 (0.00%) 0 | | |
| Psychiatric disorders Eating disorder subjects affected / exposed occurrences (all) Irritability alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 27 / 74 (36.49%) 55 17 / 74 (22.97%) 27 | | |
| Musculoskeletal and connective tissue disorders Arthralgia alternative assessment type: Systematic subjects affected / exposed occurrences (all) Myalgia alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 0 / 74 (0.00%) 0 0 / 74 (0.00%) 0 | | |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Conjunctivitis | 1 / 74 (1.35%) 1 | | |

| | | | |
|-----------------------------------|------------------|--|--|
| subjects affected / exposed | 6 / 74 (8.11%) | | |
| occurrences (all) | 6 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 33 / 74 (44.59%) | | |
| occurrences (all) | 46 | | |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 74 (1.35%) | | |
| occurrences (all) | 2 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 2 / 74 (2.70%) | | |
| occurrences (all) | 2 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 74 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 30 July 2009 | To allow interim analysis of the study, if there is a request in public health interest. |
| 07 April 2010 | To address the change that the booster will be administered using the egg-derived, seasonal, trivalent MF59 adjuvanted vaccine |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported