Safety and Immunogenicity of 3 Lots of Cell-derived Subunit Influenza Vaccine as Compared to 1 Lot to Egg-derived Subunit Influenza Vaccine in Healthy Adults (>=18 to <=60)

This study has been completed.

Sponsor:	Novartis Vaccines
Collaborators:	Novartis Vaccines
Information provided by (Responsible Party):	Novartis (Novartis Vaccines)
ClinicalTrials.gov Identifier:	NCT00310804

Purpose

The present study aims to evaluate safety, tolerability and immunogenicity of three lots of Chiron's cell-derived subunit influenza vaccine in healthy adult subjects as compared to a conventional egg-derived control vaccine licensed in Europe.

Condition	Intervention	Phase
Influenza	Biological/Vaccine: Cell-Derived Trivalent Subunit Influenza Vaccine Lot 1 (cTIV) Biological/Vaccine: Cell-Derived Trivalent Subunit Influenza Vaccine Lot 2 (cTIV) Biological/Vaccine: Cell-Derived Trivalent Subunit Influenza Vaccine Lot 3 (cTIV) Biological/Vaccine: Egg-Derived Trivalent Subunit Influenza Vaccine (TIV)	Phase 3

Study Type: Interventional
Study Design: Prevention, Parallel Assignment, Single Blind (Subject), Randomized, Safety/Efficacy Study

Official Title: A Phase III, Randomized, Controlled, Observer-Blind, Multi-Center Study to Evaluate Safety, Tolerability and Immunogenicity of a Single Intramuscular Dose of Three Lots of a Trivalent Subunit Influenza Vaccine Produced in Mammalian Cell Culture Or of a Trivalent Subunit Influenza Vaccine Produced in Embryonated Hen Eggs, in Healthy Adult Subjects Aged >=18 to <=60

Further study details:

Primary Outcome Measure:

- Geometric Mean Titers After One Dose of Cell Culture-derived or the Egg-derived Influenza Vaccine in Adult Subjects [Time Frame: Day 22 postvaccination] [Designated as safety issue: No]
  The haemagglutinin Inhibition (HI) antibody titer response following 1) one dose of cTIV for each of the three lots separately and 2) one dose of cTIV (combined) compared to TIV is reported as Geometric mean titers (GMTs). The HI GMTs were evaluated using egg-derived antigen assay.
- Geometric Mean Ratios After One Dose of Cell Culture-derived or the Egg-derived Influenza Vaccine in Adult Subjects [Time Frame: Day 22 postvaccination] [Designated as safety issue: No]
  Immunogenicity was assessed in terms of Geometric Mean Ratio (GMR) following 1) one dose of cTIV for each of the three vaccine lots separately and 2) for one dose of cTIV (combined) compared to TIV, according to the CHMP criterion. The European licensure (CHMP) criterion is met if the mean geometric increase (GMR, day 22/day 1) in HI antibody titer is >2.5.
- Percentage of Subjects With HI Titers ≥40 [Time Frame: Day 22 postvaccination] [Designated as safety issue: No]
  Immunogenicity was assessed in terms of percentage of adult subjects achieving HI titers ≥40, after 1) one dose of cTIV for each of the three vaccine lots separately and 2) for one dose of cTIV (combined) compared to TIV, according to the CHMP criterion. European Licensure (CHMP) criterion is met if the percentage of subjects achieving HI titers ≥40 is >70%.
- Percentage of Subjects With Seroconversion or Significant Increase in HI Antibody Titers After One Dose of Either Cell-derived or Egg-derived Subunit Trivalent Influenza Vaccine [Time Frame: Day 22 postvaccination] [Designated as safety issue: No]
  Immunogenicity was assessed in terms of percentage of adult subjects showing seroconversion or significant increase in HI antibody titers after 1) one dose of cTIV for each of the three vaccine lots separately and 2) one dose of cTIV (combined) compared to TIV, according to the CHMP criterion. European Licensure (CHMP) criterion is met if the percentage of subjects achieving seroconversion or significant increase is >40%. As per European Licensure (CHMP) criterion seroconversion is defined as percentage of subjects with a prevaccination HI titer <10 to a postvaccination titer ≥40; whereas, significant increase is defined as HI titer ≥10 prevaccination and ≥4-fold Hi titer increase post-vaccination.

Secondary Outcome Measures:

- Number of Subjects Reporting Solicited Adverse Events After One Dose of Cell Culture-derived or the Egg-derived Influenza Vaccine. [Time Frame: Day 1 to Day 7 postvaccination] [Designated as safety issue: Yes]
  To assess the safety and tolerability in terms of number of subjects reporting solicited adverse events following one injection of 1) one dose of cTIV for each of the three vaccine lots separately and 2) for one dose of cTIV (combined) compared to TIV.
- Safety Data of Subjects Upto Six Months After One Dose of Cell Culture Derived or Egg-derived Influenza Vaccine [Time Frame: Day 1 - Day 181 postvaccination] [Designated as safety issue: Yes]
  Additional safety data from day 1 through day 181 after one dose of cTIV (combined) or TIV in terms of serious adverse events (SAEs), adverse events (AEs) necessitating a physician's visit and/or resulting in premature subject's withdrawal from study is reported.

Enrollment: 1200
Study Start Date: September 2005
Primary Completion Date: October 2005
Study Completion Date: April 2006

Arms	Assigned Interventions
Experimental: cTIV_lot 1	Biological/Vaccine: Cell-Derived Trivalent Subunit Influenza Vaccine Lot 1 (cTIV) One single 0.5ml intramuscular injection of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 1
Experimental: cTIV_lot 2	Biological/Vaccine: Cell-Derived Trivalent Subunit Influenza Vaccine Lot 2 (cTIV) One single 0.5ml intramuscular injection of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 2
Experimental: cTIV_lot 3	Biological/Vaccine: Cell-Derived Trivalent Subunit Influenza Vaccine Lot 3 (cTIV) One single 0.5ml intramuscular injection of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 3
Active Comparator: TIV group	Biological/Vaccine: Egg-Derived Trivalent Subunit Influenza Vaccine (TIV) One single 0.5ml intramuscular injection of Egg Derived Trivalent Subunit Influenza Vaccine (TIV).

Eligibility

Ages Eligible for Study: 18 Years to 60 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: Yes

Criteria

Inclusion Criteria:

1. 18 to <61 years of age
2. mentally competent to understand the nature, the scope and the consequences of the study
3. able and willing to give written informed consent prior to study entry
4. in good health as determined by:
    a. medical history,
    b. physical examination,
    c. clinical judgment of the Investigator.

Exclusion Criteria:

1. unwilling or unable to give written informed consent to participate in the study
2. participation in another clinical trial of an investigational agent within 90 days prior to Visit 1 and throughout the entire study

3. currently experiencing an acute infectious disease
4. any serious disease, such as, for example:
    a. cancer,
    b. autoimmune disease (including rheumatoid arthritis),
    c. advanced arteriosclerotic disease or complicated diabetes mellitus,
    d. chronic obstructive pulmonary disease (COPD) requiring oxygen therapy,
    e. acute or progressive hepatic disease,
    f. acute or progressive renal disease,
    g. congestive heart failure
5. surgery planned during the study period
6. bleeding diathesis
7. history of hypersensitivity to any component of the study medication or chemically related substances
8. history of any anaphylaxis, serious vaccine reactions, or allergy to any of the vaccine component
9. known or suspected impairment/alteration of immune function, for example resulting from:
    a. receipt of immunosuppressive therapy (any corticosteroid therapy or cancer chemotherapy),
    b. receipt of immunostimulants,
    c. receipt of parenteral immunoglobulin preparation, blood products, and/or plasma derivates within 3 months prior to Visit 1 or planned during the full length of the study,
    d. high risk for developing an immunocompromising disease
10. history of drug or alcohol abuse
11. laboratory-confirmed influenza disease within 6 months prior to Visit 1
12. receipt of influenza vaccine within 6 months prior to Visit 1
13. receipt of another vaccine within 60 days prior to Visit 1, or planned vaccination within 3 weeks following study vaccination
14. any acute respiratory disease or infections requiring systemic antibiotic or antiviral therapy (chronic antibiotic therapy for urinary tract prophylaxis is acceptable) or experienced fever (i.e., axillary temperature ≥ 38 degree C) within 5 days prior to Visit 1
15. if female, pregnant or breastfeeding
16. if female, refusal to use a reliable contraceptive method during the three weeks following vaccination
17. planned relocation abroad during the study period
18. any condition that, in the opinion of the Investigator, might interfere with the evaluation of the study objectives.

Contacts and Locations

Locations

Lithuania

2nd Department of Internal Diseases, Panevezys Hospital,
Panevezys, Lithuania

Dept. Infectious Diseases and Microbiology of Vilnius University
Vilnius, Lithuania

Investigators

Study Chair:	Novartis Vaccines	Novartis Vaccines & Diagnostics

More Information

Results Publications:

Ambrozaitis A, Groth N, Bugarini R, Sparacio V, Podda A, Lattanzi M. A novel mammalian cell-culture technique for consistent production of a well-tolerated and immunogenic trivalent subunit influenza vaccine. Vaccine. 2009 Oct 9;27(43):6022-9. doi: 10.1016/j.vaccine.2009.07.083. Epub 2009 Aug 8.

Responsible Party: Novartis Vaccines
Study ID Numbers: V58P9
EUDRACT: 2005-002257-47
Health Authority: Lithuania: State Medicine Control Agency - Ministry of Health

Study Results

Participant Flow

Recruitment Details	Subjects were enrolled from a single site in Lithuania.
Pre-Assignment Details	All participants enrolled were included in the trial.

Reporting Groups

	Description
cTIV (Combined)	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine from one of three vaccine Lots (Lot1, Lot2 or Lot3).
TIV Group	Subjects in this group received one dose of Egg derived Trivalent Subunit Influenza Vaccine (TIV).

Overall Study

	cTIV (Combined)	TIV Group
Started	1029	171
Completed	1024	171
Not Completed	5	0
Lost to Follow-up	2	0
Withdrawal by Subject	3	0

Baseline Characteristics

Reporting Groups

	Description
cTIV (Combined)	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine from one of three vaccine Lots (Lot1, Lot2 or Lot3).
TIV Group	Subjects in this group received one dose of Egg Derived Trivalent Subunit Influenza Vaccine (TIV).

Baseline Measures

	cTIV (Combined)	TIV Group	Total
Number of Participants	600	100	700
Age, Continuous [units: years] Mean (Standard Deviation)	27.3 (11.1)	26.9 (11.5)	27.2 (11.1)
Gender, Male/Female [units: participants]			
Female	321	58	379
Male	279	42	321
Region of Enrollment Lithuania [units: participants]	600	100	700

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Geometric Mean Titers After One Dose of Cell Culture-derived or the Egg-derived Influenza Vaccine in Adult Subjects
Measure Description	The haemagglutinin Inhibition (HI) antibody titer response following 1. one dose of cTIV for each of the three lots separately and 2. one dose of cTIV (combined) compared to TIV is reported as Geometric mean titers (GMTs). The HI GMTs were evaluated using egg-derived antigen assay.
Time Frame	Day 22 postvaccination
Safety Issue?	No

Analysis Population Description

This analysis was done on per protocol (PP) population defined as all subjects who received all the relevant doses of vaccine correctly, and provided evaluable serum samples at the relevant time points, and had no major protocol deviation.

Reporting Groups

	Description
cTIV_lot1	Subjects in this group received one dose of Cell-Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 1.
cTIV_lot 2	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 2
cTIV_lot3	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 3.
cTIV (Combined)	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine from one of three vaccine Lots (Lot1, Lot2 or Lot3).
TIV Group	Subjects in this group received one dose of Egg Derived Trivalent Subunit Influenza Vaccine (TIV).

Measured Values

	cTIV_lot1	cTIV_lot 2	cTIV_lot3	cTIV (Combined)	TIV Group
Number of Participants Analyzed	198	193	198	589	98
Geometric Mean Titers After One Dose of Cell Culture-derived or the Egg-derived Influenza Vaccine in Adult Subjects [units: Titers] Geometric Mean (95% Confidence Interval)					
A/H3N2 strain (day 1)	12 (11 to 14)	15 (13 to 17)	16 (14 to 19)	14 (13 to 16)	15 (12 to 18)
A/H3N2 strain (day 22)	175 (147 to 207)	171 (144 to 203)	158 (133 to 188)	168 (152 to 185)	186 (146 to 236)
A/H1N1 strain (day 1)	20 (17 to 24)	20 (17 to 25)	21 (17 to 25)	20 (18 to 22)	22 (18 to 29)
A/H1N1 strain (day 22)	390 (326 to 466)	364 (303 to 436)	366 (306 to 437)	373 (335 to 415)	329 (253 to 428)
B strain (day 1)	13 (11 to 15)	17 (14 to 19)	14 (12 to 16)	14 (13 to 16)	16 (13 to 20)
B strain (day 22)	131 (113 to 151)	157 (136 to 182)	128 (111 to 148)	138 (126 to 151)	124 (99 to 154)

2. Primary Outcome Measure:

Measure Title	Geometric Mean Ratios After One Dose of Cell Culture-derived or the Egg-derived Influenza Vaccine in Adult Subjects

Measure Description	Immunogenicity was assessed in terms of Geometric Mean Ratio (GMR) following 1. one dose of cTIV for each of the three vaccine lots separately and 2. for one dose of cTIV (combined) compared to TIV, according to the CHMP criterion. The European licensure (CHMP) criterion is met if the mean geometric increase (GMR, day 22/day 1) in HI antibody titer is >2.5.
Time Frame	Day 22 postvaccination
Safety Issue?	No

Analysis Population Description

The analysis was performed as PP dataset.

Reporting Groups

	Description
cTIV_lot1	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 1.
cTIV_lot 2	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 2.
cTIV_lot3	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 3.
cTIV (Combined)	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine from one of three vaccine Lots (Lot1, Lot2 or Lot3).
TIV Group	Subjects in this group received one dose of Egg-Derived Trivalent Subunit Influenza Vaccine(TIV).

Measured Values

	cTIV_lot1	cTIV_lot 2	cTIV_lot3	cTIV (Combined)	TIV Group
Number of Participants Analyzed	198	193	198	589	98
Geometric Mean Ratios After One Dose of Cell Culture-derived or the Egg-derived Influenza Vaccine in Adult Subjects [units: Ratio] Geometric Mean (95% Confidence Interval)					
A/H1N1 strain (Day22/Day1)	20 (16 to 24)	18 (14 to 22)	18 (14 to 22)	18 (16 to 21)	15 (11 to 20)
A/H3N2 strain (Day22/Day1)	14 (12 to 17)	11 (9.55 to 14)	9.92 (8.28 to 12)	12 (11 to 13)	12 (9.57 to 16)
B strain (Day22/Day1)	10 (8.59 to 12)	9.42 (7.97 to 11)	9.37 (7.94 to 11)	9.63 (8.71 to 11)	7.53 (5.88 to 9.65)

3. Primary Outcome Measure:

Measure Title	Percentage of Subjects With HI Titers ≥40
Measure Description	Immunogenicity was assessed in terms of percentage of adult subjects achieving HI titers ≥40, after 1. one dose of cTIV for each of the three vaccine lots separately and 2. for one dose of cTIV (combined) compared to TIV, according to the CHMP criterion. European Licensure (CHMP) criterion is met if the percentage of subjects achieving HI titers ≥40 is >70%.
Time Frame	Day 22 postvaccination
Safety Issue?	No

Analysis Population Description

This analysis was done on PP population.

Reporting Groups

	Description
cTIV_lot 1	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 1.
cTIV_lot 2	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 2.
cTIV_lot 3	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 3.
cTIV (Combined)	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine from one of three vaccine Lots (Lot1, Lot2 or Lot3).
TIV Group	Subjects in this group received one dose of Egg Derived Trivalent Subunit Influenza Vaccine (TIV).

Measured Values

	cTIV_lot 1	cTIV_lot 2	cTIV_lot 3	cTIV (Combined)	TIV Group
Number of Participants Analyzed	198	193	198	589	98
Percentage of Subjects With HI Titers ≥40 [units: Percentages] Number (95% Confidence Interval)					
A/H1N1 strain (day 1)	36 (29 to 43)	38 (31 to 46)	34 (27 to 41)	36 (32 to 40)	38 (28 to 48)
A/H1N1 strain (day 22)	97 (94 to 99)	97 (93 to 99)	94 (90 to 97)	96 (94 to 98)	97 (91 to 99)
A/H3N2 strain (day 1)	19 (14 to 25)	31 (24 to 38)	28 (22 to 35)	26 (22 to 30)	28 (19 to 37)
A/H3N2 strain (day 22)	92 (88 to 96)	93 (88 to 96)	91 (86 to 95)	92 (90 to 94)	97 (91 to 99)
B strain (day 1)	25 (19 to 32)	31 (25 to 38)	25 (19 to 31)	27 (23 to 31)	31 (22 to 41)

	cTIV_lot 1	cTIV_lot 2	cTIV_lot 3	cTIV (Combined)	TIV Group
B strain (day 22)	92 (88 to 96)	94 (90 to 97)	93 (89 to 96)	93 (91 to 95)	93 (86 to 97)

4. Primary Outcome Measure:

Measure Title	Percentage of Subjects With Seroconversion or Significant Increase in HI Antibody Titers After One Dose of Either Cell-derived or Egg-derived Subunit Trivalent Influenza Vaccine
Measure Description	Immunogenicity was assessed in terms of percentage of adult subjects showing seroconversion or significant increase in HI antibody titers after 1. one dose of cTIV for each of the three vaccine lots separately and 2. one dose of cTIV (combined) compared to TIV, according to the CHMP criterion. European Licensure (CHMP) criterion is met if the percentage of subjects achieving seroconversion or significant increase is >40%. As per European Licensure (CHMP) criterion seroconversion is defined as percentage of subjects with a prevaccination HI titer <10 to a postvaccination titer ≥40; whereas, significant increase is defined as HI titer ≥10 prevaccination and ≥4-fold Hi titer increase post-vaccination.
Time Frame	Day 22 postvaccination
Safety Issue?	No

Analysis Population Description

This analysis was done on PP population.

Reporting Groups

	Description
cTIV_lot1	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 1.
cTIV_lot 2	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 2.
cTIV_lot3	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from lot 3.
cTIV (Combined)	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine from one of three vaccine Lots (Lot1, Lot2 or Lot3).
TIV Group	Subjects in this group received one dose of Egg Derived Trivalent Subunit Influenza Vaccine (TIV).

Measured Values

	cTIV_lot1	cTIV_lot 2	cTIV_lot3	cTIV (Combined)	TIV Group
Number of Participants Analyzed	198	193	198	589	98
Percentage of Subjects With Seroconversion or Significant Increase in HI Antibody Titers After One Dose of Either Cell-derived or Egg-derived Subunit Trivalent Influenza Vaccine [units: Percentages] Number (95% Confidence Interval)					
A/H1N1 strain	80 (74 to 86)	81 (75 to 86)	82 (76 to 87)	81 (78 to 84)	76 (66 to 84)
A/H3N2 strain	84 (78 to 89)	79 (72 to 84)	78 (71 to 83)	80 (77 to 83)	88 (80 to 94)
B strain	79 (72 to 84)	81 (75 to 87)	80 (74 to 85)	80 (77 to 83)	70 (60 to 79)

5. Secondary Outcome Measure:

Measure Title	Number of Subjects Reporting Solicited Adverse Events After One Dose of Cell Culture-derived or the Egg-derived Influenza Vaccine.
Measure Description	To assess the safety and tolerability in terms of number of subjects reporting solicited adverse events following one injection of 1. one dose of cTIV for each of the three vaccine lots separately and 2. for one dose of cTIV (combined) compared to TIV.
Time Frame	Day 1 to Day 7 postvaccination
Safety Issue?	Yes

Analysis Population Description

Analysis was done on safety dataset.

Reporting Groups

	Description
cTIV_lot1	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 1.
cTIV_lot2	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 2.
cTIV_lot3	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine (cTIV) from Lot 3.

	Description
cTIV (Combined)	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine from one of three vaccine Lots (Lot1, Lot2 or Lot3).
TIV Group	Subjects in this group received one dose of Egg Derived Trivalent Subunit Influenza Vaccine (TIV).

Measured Values

	cTIV_lot1	cTIV_lot2	cTIV_lot3	cTIV (Combined)	TIV Group
Number of Participants Analyzed	200	199	200	599	100
Number of Subjects Reporting Solicited Adverse Events After One Dose of Cell Culture-derived or the Egg-derived Influenza Vaccine. [units: subjects]					
Any Local	57	40	37	134	16
Injection site ecchymosis	6	7	3	16	5
Injection site erythema	32	18	16	66	8
Injection site induration	11	13	6	30	6
Injection site swelling	10	7	6	23	4
Injection site pain	33	23	24	80	10
Any Systemic	62	53	55	170	29
Chills	18	13	10	41	9
Malaise	36	29	26	91	15
Myalgia	14	13	11	38	8
Arthralgia	6	8	5	19	2
Headache	32	31	31	94	16
Sweat	8	15	11	34	4
Fatigue	39	29	32	100	17
Fever (>=38C)	1	1	2	4	1
Other	13	3	15	31	9
Stayed home due to reaction	7	3	7	17	3
Analgesic Antipyretic medication used	10	2	10	22	8

6. Secondary Outcome Measure:

Measure Title	Safety Data of Subjects Upto Six Months After One Dose of Cell Culture Derived or Egg-derived Influenza Vaccine
Measure Description	Additional safety data from day 1 through day 181 after one dose of cTIV (combined) or TIV in terms of serious adverse events (SAEs), adverse events (AEs) necessitating a physician's visit and/or resulting in premature subject's withdrawal from study is reported.
Time Frame	Day 1 - Day 181 postvaccination
Safety Issue?	Yes

Analysis Population Description

This analysis was done on safety dataset.

Reporting Groups

	Description
cTIV (Combined) Day 1 to Day 22	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine from one of three vaccine Lots (Lot 1, Lot2 or Lot3).
cTIV (Combined) Day 23 to Day 181	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine from one of three vaccine Lots (Lot1, Lot2 or Lot3).
TIV Group Day 1 to Day 22	Subjects in this group received one dose of Egg Derived Trivalent Subunit Influenza Vaccine (TIV).
TIV Group Day 23 to Day 181	Subjects in this group received one dose of Egg Derived Trivalent Subunit Influenza Vaccine (TIV).

Measured Values

	cTIV (Combined) Day 1 to Day 22	cTIV (Combined) Day 23 to Day 181	TIV Group Day 1 to Day 22	TIV Group Day 23 to Day 181
Number of Participants Analyzed	599	571	100	97
Safety Data of Subjects Upto Six Months After One Dose of Cell Culture Derived or Egg-derived Influenza Vaccine [units: subjects]				
Any AEs	74	62	13	6
At least possibly related AEs	45	1	10	0
Serious AEs	2	14	0	2
At least possibly related SAEs	0	0	0	0

	cTIV (Combined) Day 1 to Day 22	cTIV (Combined) Day 23 to Day 181	TIV Group Day 1 to Day 22	TIV Group Day 23 to Day 181
Death	0	1	0	0
AE leading to withdrawal	0	1	0	0

Reported Adverse Events

Time Frame	Through out the study period
Additional Description	Post-injection solicited adverse events were collected from Day1-7. Other AE's and SAEs were collected through out the study period (Day 1 to 6 months). In cTIV(Combined group),599/600 subjects were included in safety dataset as one subject did not receive the vaccination and withdrew on day 1.

Reporting Groups

	Description
cTIV (Combined)	Subjects in this group received one dose of Cell Derived Trivalent Subunit Influenza Vaccine from one of three vaccine Lots (Lot1, Lot2 or Lot3).
TIV Group	Subjects in this group received one dose of Egg Derived Trivalent Subunit Influenza Vaccine (TIV).

Serious Adverse Events

	cTIV (Combined)	TIV Group
	Affected/At Risk (%)	Affected/At Risk (%)
Total	16/599 (2.67%)	2/100 (2%)
Ear and labyrinth disorders		
Vestibular disorder [A] *	1/599 (0.17%)	0/100 (0%)
Gastrointestinal disorders		
Diarrhoea [A] *	1/599 (0.17%)	0/100 (0%)
Hepatobiliary disorders		
Cholelithiasis [A] *	1/599 (0.17%)	0/100 (0%)

	cTIV (Combined)	TIV Group
	Affected/At Risk (%)	Affected/At Risk (%)
Infections and infestations		
Influenza [A] *	4/599 (0.67%)	1/100 (1%)
Rhinitis [A] *	1/599 (0.17%)	0/100 (0%)
Injury, poisoning and procedural complications		
Injury Asphyxiation [A] *	1/599 (0.17%)	0/100 (0%)
Lower Limb Fracture [A] *	1/599 (0.17%)	0/100 (0%)
Spinal Compression Fracture [A] *	1/599 (0.17%)	0/100 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Breast Cancer [A] *	1/599 (0.17%)	0/100 (0%)
Nervous system disorders		
Vertebrobasilar Insufficiency [A] *	1/599 (0.17%)	0/100 (0%)
Psychiatric disorders		
Schizoaffective disorder [A] *	1/599 (0.17%)	0/100 (0%)
Schizoid Personality Disorder [A] *	0/599 (0%)	1/100 (1%)
Reproductive system and breast disorders		
Uterine Polyp [A] *	1/599 (0.17%)	0/100 (0%)
Vascular disorders		
Essential Hypertension [A] *	1/599 (0.17%)	0/100 (0%)
Varicose Vein [A] *	1/599 (0.17%)	0/100 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (Unspecified)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	cTIV (Combined)	TIV Group
	Affected/At Risk (%)	Affected/At Risk (%)
Total	237/599 (39.57%)	35/100 (35%)
General disorders		
Chills [A] †	41/599 (6.84%)	9/100 (9%)
Fatigue [A] †	100/599 (16.69%)	17/100 (17%)
Injection Site Erythema [A] †	66/599 (11.02%)	8/100 (8%)
Injection Site Induration [A] †	30/599 (5.01%)	6/100 (6%)
Injection Site Pain [A] †	80/599 (13.36%)	10/100 (10%)
Malaise [A] †	92/599 (15.36%)	15/100 (15%)
Infections and infestations		
Rhinitis [A] †	19/599 (3.17%)	6/100 (6%)
Musculoskeletal and connective tissue disorders		
Myalgia [A] †	38/599 (6.34%)	8/100 (8%)
Nervous system disorders		
Headache [A] †	95/599 (15.86%)	16/100 (16%)
Skin and subcutaneous tissue disorders		
Hyperhidrosis [A] *	34/599 (5.68%)	4/100 (4%)

† Indicates events were collected by systematic assessment.

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA (Unspecified)

Limitations and Caveats

Because of potential issues related to Good Clinical Practice (GCP), data from one of the sites were not used in the analyses.

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is more than 60 days but less than or equal to 180 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

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