The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: 109821 (FluAS25-010 EXT:005 Y1)

Title: Immunogenicity and safety of GSK Biologicals adjuvanted influenza vaccine administered to adults over 65 years previously vaccinated with the same vaccine, compared to Fluarix™.
FluAS25 (Flu-1): GlaxoSmithKline (GSK) Biologicals' AS25 adjuvanted influenza vaccine.
Fluarix™ (Flu-2): GSK Biologicals' licensed influenza vaccine.

Rationale: The aim of this study was to evaluate the safety of Flu-1 vaccine after repeated vaccination. The subjects previously enrolled in study FluAS25-005 (104888) study received a dose with the 2007-2008 season formulation of the vaccines. Flu-2 was used as control.

Phase: III

Study Period: 15 October 2007 to 04 June 2008.

Study Design: Multi-country (US and Europe), multi-center controlled study; the study was observer blind for subjects ≥ 65 years and open for subjects aged 18-40 years.

Centers: Multi-center study with 29 centers: 9 in the United States, 1 in Belgium, 12 in Germany, and 7 in Norway.

Indication: Immunization against influenza.

Treatment: The study groups within each age stratum (18-40 years*, 65-74 years and ≥ 75 years) were as follows:

- Flu-1 Group: subjects who had received 1 dose of Flu-1 vaccine during the 104888 study, received 1 dose of Flu-1 vaccine.
- Flu-2 Group: subjects who had received 1 dose of Flu-2 vaccine during the 104888 study, received 1 dose of Flu-2 vaccine.

Subjects were administered the vaccine dose by intramuscular injection in the deltoid region of the non-dominant arm.
For some data analyses, the 65-74 years and 75+ years subjects were pooled into the 65+ years age sub-group.
*As per protocol, none of the subjects aged 18 to 40 years should have been allocated to the Flu-1 Group.

Objectives:
To evaluate the safety of repeated vaccination with Flu-1 vaccine in elderly subjects (previously enrolled in the ≥ 65 years age sub-group), during the 21 days following the intramuscular administration of the vaccine. Flu-2 administered to young adults (previously enrolled in the 18-40 years age sub-group) and to elderly subjects (previously enrolled in the ≥ 65 years age sub-group) was used as reference.

Primary Outcome/Efficacy Variable:

- Occurrence, intensity, duration and relationship to vaccination of solicited local and general signs and symptoms during a 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after vaccination, in each group.
- Occurrence, intensity, duration* and relationship to vaccination of unsolicited adverse events (AEs) during a 21-day follow-up period (i.e. day of vaccination and 20 subsequent days) after vaccination, in each group.

*Duration of unsolicited symptoms reported during the 21-day follow-up period was not analyzed.

Secondary Outcome/Efficacy Variable(s):
Safety

- Occurrence and relationship to vaccination of serious adverse events (SAEs) during the entire study period (up to Day 180) in each group.
- Occurrence, intensity, duration† and relationship to vaccination of medically significant conditions prompting emergency room visits, hospitalizations or physician visits and that are not routine visits for physical examination or vaccination, during the entire study period (up to Day 180) in each group††.

†Duration of medically significant conditions during the 21-day follow-up period was not analyzed.
††It was decided to analyze the medically significant conditions as all adverse events that resulted in a medically attended visit instead, because this was considered to be an objective approach.

Humoral immune response
Observed variable:

- At Days 0 and 21: serum haemagglutination-inhibition (HI) antibody titer, against each of the 3 vaccine strains in each group.

Derived variables:

- Geometric mean titers (GMTs) of HI antibodies at Day 0 and 21.
- Seroconversion rates (SCR)* at Day 21.

- Seroconversion factors (SCF)** at Day 21.
- Seroprotection rates (SPR)*** at Day 0 and 21.

* SCR was defined as the percentage of vaccinees who had either a pre-vaccination titer <1:10 and a post-vaccination titer ≥1:40 or a pre-vaccination titer ≥1:10 and at least a four-fold increase in post-vaccination titer.
**SCF was defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0.
***SPR was defined as the percentage of vaccinees with a serum HI titer ≥1:40 that is usually accepted as indicating protection.

CMI response (only for subjects enrolled in the CMI subset)
CMI response [interferon-γ (IFN-γ), interleukin-2 (IL-2), cluster of differentiation-40 ligand (CD40L), tumor necrosis factor alpha (TNF-α)]
Observed variables:

- Frequency of cytokine-positive CD4/CD8 cells per 10^6 in tests producing at least two different cytokines (CD40L, IL-2, TNF-α, IFN-γ) at Day 0 and 21.
- Frequency of cytokine-positive CD4/CD8 cells per 10^6 in tests producing at least CD40L and another signal molecule (IL-2, IFN-γ, TNF-α) at Day 0 and 21.
- Frequency of cytokine-positive CD4/CD8 cells per 10^6 in tests producing at least IL-2 and another signal molecule (CD40L, IFN-γ, TNF-α) at Day 0 and 21.
- Frequency of cytokine-positive CD4/CD8 cells per 10^6 in tests producing at least IFN-γ and another signal molecule (IL-2, CD40L, TNF-α) at Day 0 and 21.
- Frequency of cytokine-positive CD4/CD8 cells per 10^6 in tests producing at least TNF-α and another signal molecule (IL-2, CD40L, IFN-γ) at Day 0 and 21.

Derived variables:

- For each test, geometric mean (GM) of specific influenza CD4/CD8 T lymphocytes at Day 0 and 21.

Statistical Methods:
The analyses were performed on the Total Vaccinated Cohort, on the According-To-Protocol (ATP) cohort for immunogenicity HI and on the ATP cohort for immunogenicity CMI.

- The Total Vaccinated Cohort included all subjects with study vaccine administered.
- The ATP cohort for immunogenicity HI included all evaluable subjects who met all eligibility criteria, who complied with the procedures and intervals defined in the protocol up to the end of the active study phase, with no elimination criteria during the study, for whom data concerning immunogenicity measures (HI) were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination.
- The ATP cohort of immunogenicity CMI included a subset of subjects from the ATP Cohort for immunogenicity HI. This included subjects for whom at least one frequency of immune response marker-positive CD4/CD8 result was available 21 days after vaccination.

Analysis of Immunogenicity:
The analysis of immunogenicity was performed on the ATP cohort for immunogenicity HI and ATP cohort for immunogenicity CMI.
For each treatment group, GMT with 95% CI at days 0 and 21, seropositivity rates and SPR with exact 95% CI at days 0 and 21, SCR and SCF with 95% CI at Day 21 were calculated separately for the age sub-groups (for subjects previously enrolled in the 18-40 years age sub-group, and for those previously enrolled in the ≥ 65 years age sub-group, further stratified in 2 age sub-groups: 65-74 years and ≥ 75 years). Antibody titers below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculation.
For the age sub-groups defined above, the frequency of influenza-specific immune marker-positive CD4/CD8 T-lymphocytes was summarized (descriptive statistics) for each vaccine group at days 0 and 21, for each different test and for separate vaccine strains.

Analysis of Safety
The analysis was based on the Total Vaccinated Cohort.
The percentage of subjects reporting each individual solicited local and general symptom during the 7-day (Days 0-6) solicited follow-up period was tabulated with exact 95% CI. The same tabulation was performed for grade 3 symptoms and for general symptoms assessed by the investigators as related to vaccination. Moreover, the number of days the subjects experienced each solicited local and general adverse event was tabulated.
The proportion of subjects with at least one report of unsolicited AE classified by the Medical Dictionary for Regulatory Activities (MedDRA) and reported up to 21 days after vaccination was tabulated.

The proportion of subjects with at least one report of unsolicited adverse event that resulted in a medically attended visit classified by MedDRA and reported within the 21-day (Days 0 - 20) post-vaccination period and between Day 21 and Day 179 was tabulated.
The same tabulation was performed for grade 3 unsolicited adverse events and for adverse events with a relationship to vaccination.
SAEs were also tabulated according to MedDRA preferred terms during the entire study period.

Study Population: A healthy man or woman who had been enrolled in the ≥ 65 years age sub-group or in the 18-40 years age sub-group in study FluAS25-005 (104888). Women had to be of non-childbearing potential or, if of childbearing potential, they had practiced adequate contraception for 30 days prior to vaccination, had had a negative pregnancy test and had agreed to continue such precautions for 2 months after vaccination. Written informed consent was obtained prior to study start.

Number of subjects	**65-74y**		**75y+**		**65y+**	
	Flu-1 Group	**Flu-2 Group**	**Flu-1 Group**	**Flu-2 Group**	**Flu-1 Group**	**Flu-2 Group**
Planned, N	442	450	295	290	737	740
Randomized, N (Total Vaccinated Cohort)	268	286	207	202	475	488
Completed at Day 21, n (%)	267 (99.6)	285 (99.7)	205 (99.0)	201 (99.5)	472 (99.4)	486 (99.6)
Total Number Subjects Withdrawn, n (%)	1 (0.4)	1 (0.3)	2 (1.0)	1 (0.5)	3 (0.6)	2 (0.4)
Withdrawn due to Adverse Events, n (%)	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.5)	2 (0.4)	1 (0.2)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	0 (0.0)	1 (0.3)	1 (0.5)	0 (0.0)	1 (0.2)	1 (0.2)
Demographics	**Flu-1 Group**	**Flu-2 Group**	**Flu-1 Group**	**Flu-2 Group**	**Flu-1 Group**	**Flu-2 Group**
N (Total Vaccinated Cohort)	268	286	207	202	475	488
Females: Males	136:132	155:131	112:95	98:104	248:227	253:235
Mean Age, years (SD)	69.7 (2.57)	69.5 (2.49)	79.1 (3.41)	79.5 (3.82)	73.8 (5.50)	73.7 (5.80)
Caucasian/European heritage, n (%)	266 (99.3)	284 (99.3)	206 (99.5)	201 (99.5)	472 (99.4)	485 (99.4)

Number of subjects	**18-40y**
	Flu-2 Group
Planned, N	490
Randomized, N (Total Vaccinated Cohort)	289
Completed at Day 21, n (%)	288 (99.7)
Total Number Subjects Withdrawn, n (%)	1 (0.3)
Withdrawn due to Adverse Events, n (%)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable
Withdrawn for other reasons, n (%)	1 (0.3)
Demographics	**Flu-2 Group**
N (Total Vaccinated Cohort)	289
Females: Males	167:122
Mean Age, years (SD)	30.9 (6.64)
White-Caucasian/European heritage, n (%)	282 (97.6)

The double border indicates that the 65y+ age sub-group results from the pooling of the 65-74y and 75y+ age sub-groups.

Primary Efficacy Results: Number (percentage) of subjects reporting solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated Cohort)

Symptom	**Intensity**	**65y+**										**18-40y**				
		Flu-1 Group					**Flu-2Group**					**Flu-2 Group**				
		N	**n**	**%**	95% **CI**		**N**	**n**	**%**	95% **CI**		**N**	**n**	**%**	95% **CI**	
					LL	**UL**				**LL**	**UL**				**LL**	**UL**
Ecchymosis	>20 mm	472	7	1.5	0.6	3.0	487	7	1.4	0.6	2.9	288	2	0.7	0.1	2.5
	>100 mm	472	0	0.0	0.0	0.8	487	0	0.0	0.0	0.8	288	0	0.0	0.0	1.3
Pain	Any	472	271	57.4	52.8	61.9	487	76	15.6	12.5	19.1	288	170	59.0	53.1	64.8
	Grade 3	472	2	0.4	0.1	1.5	487	0	0.0	0.0	0.8	288	0	0.0	0.0	1.3
Redness	>20 mm	472	111	23.5	19.8	27.6	487	14	2.9	1.6	4.8	288	16	5.6	3.2	8.9
	>100 mm	472	12	2.5	1.3	4.4	487	0	0.0	0.0	0.8	288	0	0.0	0.0	1.3

Swelling	>20 mm	472	44	9.3	6.9	12.3	487	8	1.6	0.7	3.2	288	7	2.4	1.0	4.9
	>100 mm	472	1	0.2	0.0	1.2	487	0	0.0	0.0	0.8	288	0	0.0	0.0	1.3

N = number of subjects with the documented dose
n (%) = number (percentage) of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Any: occurrence of any local symptom regardless of their intensity grade
Grade 3 Pain: considerable pain at rest, which prevented normal everyday activities

Primary Efficacy Results: Number (percentage) of subjects reporting solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated Cohort)

Symptom	**Intensity/ Relationship**	**65y+**										**18-40y**				
		Flu-1 Group					**Flu-2 Group**					**Flu-2 Group**				
		N	**n**	**%**	95% **CI**		**N**	**N**	**%**	95% **CI**		**N**	**n**	**%**	95% **CI**	
					LL	**UL**				**LL**	**UL**				**LL**	**UL**
Arthralgia	Any	472	80	16.9	13.7	20.6	487	34	7.0	4.9	9.6	288	23	8.0	5.1	11.7
	Grade 3	472	2	0.4	0.1	1.5	487	0	0.0	0.0	0.8	288	1	0.3	0.0	1.9
	Related	472	65	13.8	10.8	17.2	487	20	4.1	2.5	6.3	288	22	7.6	4.8	11.3
Fatigue	Any	472	131	27.8	23.8	32.0	487	46	9.4	7.0	12.4	288	71	24.7	19.8	30.1
	Grade 3	472	4	0.8	0.2	2.2	487	0	0.0	0.0	0.8	288	1	0.3	0.0	1.9
	Related	472	109	23.1	19.4	27.2	487	29	6.0	4.0	8.4	288	54	18.8	14.4	23.7
Headache	Any	472	102	21.6	18.0	25.6	487	49	10.1	7.5	13.1	288	54	18.8	14.4	23.7
	Grade 3	472	4	0.8	0.2	2.2	487	1	0.2	0.0	1.1	288	1	0.3	0.0	1.9
	Related	472	87	18.4	15.0	22.2	487	37	7.6	5.4	10.3	288	39	13.5	9.8	18.0
Myalgia	Any	472	132	28.0	24.0	32.3	487	51	10.5	7.9	13.5	288	70	24.3	19.5	29.7
	Grade 3	472	4	0.8	0.2	2.2	487	0	0.0	0.0	0.8	288	1	0.3	0.0	1.9
	Related	472	116	24.6	20.8	28.7	487	38	7.8	5.6	10.6	288	64	22.2	17.6	27.5
Nausea	Any	472	35	7.4	5.2	10.2	487	23	4.7	3.0	7.0	288	17	5.9	3.5	9.3
	Grade 3	472	2	0.4	0.1	1.5	487	0	0.0	0.0	0.8	288	0	0.0	0.0	1.3
	Related	472	29	6.1	4.2	8.7	487	15	3.1	1.7	5.0	288	13	4.5	2.4	7.6
Shivering	Any	472	95	20.1	16.6	24.0	487	31	6.4	4.4	8.9	288	31	10.8	7.4	14.9
	Grade 3	472	5	1.1	0.3	2.5	487	0	0.0	0.0	0.8	288	0	0.0	0.0	1.3
	Related	472	88	18.6	15.2	22.5	487	24	4.9	3.2	7.2	288	28	9.7	6.6	13.7
Fever (Orally)	≥38.0°C	472	17	3.6	2.1	5.7	487	0	0.0	0.0	0.8	288	1	0.3	0.0	1.9
	>40.0°C	472	0	0.0	0.0	0.8	487	0	0.0	0.0	0.8	288	0	0.0	0.0	1.3
	Related	472	15	3.2	1.8	5.2	487	0	0.0	0.0	0.8	288	1	0.3	0.0	1.9

N = number of subjects with the documented dose
n (%) = number (percentage) of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Any: occurrence of any general symptom regardless of their intensity grade or relationship to vaccination.
Grade 3 Symptoms: symptoms that prevented normal activity
Related = general symptom assessed by the investigator as causally related to the study vaccination

Primary Efficacy Results: Number of days with any grade of local symptoms during the 7-day post-vaccination period (Total Vaccinated cohort)

Solicited symptom	**Sub-group**	**Group**	**N**	**Mean**
Ecchymosis	65y+	Flu-1	7	3.6
		Flu-2	7	2.9
	18-40y	Flu-2	2	4.5
Pain	65y+	Flu-1	271	2.7
		Flu-2	76	1.9
	18-40y	Flu-2	170	1.9
Redness	65y+	Flu-1	111	3.4
		Flu-2	14	2.8
	18-40y	Flu-2	16	1.7
Swelling	65y+	Flu-1	44	3.2
		Flu-2	8	1.6
	18-40y	Flu-2	5	2.4

Any grade = occurrence of any local symptom regardless of their intensity grade

N = number of subjects with the symptom
Mean = mean number of days

Primary Efficacy Results: Number of days with any grade of general symptoms during the 7-day post-vaccination period (Total Vaccinated cohort)

Solicited symptom	Sub-group	Group	N	Mean
Arthralgia	65y+	Flu-1	80	2.4
		Flu-2	34	3.5
	18-40y	Flu-2	23	2.0
Fatigue	65y+	Flu-1	131	2.1
		Flu-2	46	2.7
	18-40y	Flu-2	71	2.6
Headache	65y+	Flu-1	102	1.8
		Flu-2	49	2.2
	18-40y	Flu-2	54	1.9
Myalgia	65y+	Flu-1	132	2.2
		Flu-2	51	2.3
	18-40y	Flu-2	70	2.0
Nausea	65y+	Flu-1	35	1.3
		Flu-2	23	2.2
	18-40y	Flu-2	17	1.8
Shivering	65y+	Flu-1	95	1.5
		Flu-2	31	2.2
	18-40y	Flu-2	31	1.6
Fever (Orally)	65y+	Flu-1	17	1.1
	18-40y	Flu-2	1	1.0

Any = occurrence of any general symptom regardless of their intensity grade and relationship to vaccination
N= number of subjects with the symptom
Mean = mean number of days

Primary Efficacy Results: For results about unsolicited AEs, please refer to the safety section.

Secondary Outcome Variable(s): Seropositivity rates and GMTs for HI antibodies at Day 0 and 21 (ATP cohort for immunogenicity HI)

Vaccine strain	Sub-group	Group	Timing	N	≥ 1:10				GMT		
					n	%	95% CI		Value	95% CI	
							LL	UL		LL	UL
A/Solomon Islands	65-74y	Flu-1	PRE	253	124	49.0	42.7	55.3	11.0	9.7	12.5
			PI(D21)	255	252	98.8	96.6	99.8	131.8	114.6	151.7
		Flu-2	PRE	269	144	53.5	47.4	59.6	11.4	10.1	12.9
			PI(D21)	269	257	95.5	92.3	97.7	70.2	60.4	81.6
	75y+	Flu-1	PRE	192	88	45.8	38.6	53.2	9.9	8.7	11.3
			PI(D21)	192	179	93.2	88.7	96.3	75.0	62.9	89.5
		Flu-2	PRE	192	88	45.8	38.6	53.2	10.1	8.8	11.5
			PI(D21)	192	164	85.4	79.6	90.1	37.0	30.5	44.8
	65y+	Flu-1	PRE	445	212	47.6	42.9	52.4	10.5	9.6	11.5
			PI(D21)	447	431	96.4	94.3	97.9	103.5	92.4	115.8
		Flu-2	PRE	461	232	50.3	45.7	55.0	10.8	9.9	11.9
			PI(D21)	461	421	91.3	88.4	93.7	53.7	47.6	60.7
	18-40y	Flu-2	PRE	270	207	76.7	71.2	81.6	48.9	39.9	59.9
			PI(D21)	271	269	99.3	97.4	99.9	143.4	125.8	163.6
A/Wisconsin	65-74y	Flu-1	PRE	253	243	96.0	92.9	98.1	109.0	92.8	127.9
			PI(D21)	255	255	100	98.6	100	466.2	415.1	523.6
		Flu-2	PRE	269	255	94.8	91.4	97.1	80.8	69.0	94.6
			PI(D21)	269	269	100	98.6	100	223.9	195.4	256.5
	75y+	Flu-1	PRE	192	185	96.4	92.6	98.5	111.5	93.3	133.2
			PI(D21)	192	191	99.5	97.1	100	387.4	337.6	444.6
		Flu-2	PRE	192	184	95.8	92.0	98.2	77.8	64.4	93.9
			PI(D21)	192	191	99.5	97.1	100	209.7	178.1	246.9

	65y+	Flu-1	PRE	445	428	96.2	94.0	97.8	110.0	97.7	123.9
			PI(D21)	447	446	99.8	98.8	100	430.6	394.0	470.6
		Flu-2	PRE	461	439	95.2	92.9	97.0	79.5	70.5	89.7
			PI(D21)	461	460	99.8	98.8	100	217.9	196.3	241.8
	18-40y	Flu-2	PRE	270	268	99.3	97.3	99.9	112.5	98.1	129.0
			PI(D21)	271	271	100	98.6	100	251.2	226.4	278.8
B/Malaysia	65-74y	Flu-1	PRE	253	243	96.0	92.9	98.1	86.3	75.0	99.3
			PI(D21)	255	254	99.6	97.8	100	194.2	175.4	215.1
		Flu-2	PRE	269	265	98.5	96.2	99.6	77.8	68.9	87.7
			PI(D21)	269	269	100	98.6	100	141.2	126.7	157.5
	75y+	Flu-1	PRE	192	191	99.5	97.1	100	109.9	96.2	125.5
			PI(D21)	192	192	100	98.1	100	213.2	189.0	240.4
		Flu-2	PRE	192	189	98.4	95.5	99.7	89.7	77.4	104.0
			PI(D21)	192	191	99.5	97.1	100	169.2	148.2	193.1
	65y+	Flu-1	PRE	445	434	97.5	95.6	98.8	95.8	86.8	105.7
			PI(D21)	447	446	99.8	98.8	100	202.2	187.1	218.5
		Flu-2	PRE	461	454	98.5	96.9	99.4	82.5	75.2	90.6
			PI(D21)	461	460	99.8	98.8	100	152.3	140.0	165.6
	18-40y	Flu-2	PRE	270	261	96.7	93.8	98.5	110.5	95.9	127.2
			PI(D21)	271	270	99.6	98.0	100	209.2	188.9	231.7

N = number of subjects with available results
n (%) = number (percentage) of seropositive subjects (HI antibody titer ≥ 1:10)
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination (Day 0)
PI(D21) = post-vaccination (Day 21)

Secondary Outcome Variable(s): Seroconversion rates (SCR) for HI antibody titer at Day 21 (ATP cohort for immunogenicity HI)

Vaccine strain	**Sub-group**	**Group**	**N**	**SCR**			
				N	**%**	**95% CI**	
						LL	**UL**
A/Solomon Islands	65-74y	Flu-1	253	192	75.9	70.1	81.0
		Flu-2	269	162	60.2	54.1	66.1
	75y+	Flu-1	192	128	66.7	59.5	73.3
		Flu-2	192	76	39.6	32.6	46.9
	65y+	Flu-1	445	320	71.9	67.5	76.0
		Flu-2	461	238	51.6	47.0	56.3
	18-40y	Flu-2	270	94	34.8	29.1	40.8
A/Wisconsin	65-74y	Flu-1	253	133	52.6	46.2	58.9
		Flu-2	269	95	35.3	29.6	41.4
	75y+	Flu-1	192	93	48.4	41.2	55.7
		Flu-2	192	61	31.8	25.3	38.9
	65y+	Flu-1	445	226	50.8	46.0	55.5
		Flu-2	461	156	33.8	29.5	38.4
	18-40y	Flu-2	270	66	24.4	19.4	30.0
B/Malaysia	65-74y	Flu-1	253	51	20.2	15.4	25.6
		Flu-2	269	41	15.2	11.2	20.1
	75y+	Flu-1	192	31	16.1	11.2	22.1
		Flu-2	192	25	13.0	8.6	18.6
	65y+	Flu-1	445	82	18.4	14.9	22.3
		Flu-2	461	66	14.3	11.2	17.9
	18-40y	Flu-2	270	46	17.0	12.8	22.1

N = number of subjects with pre- and post-vaccination results available
n (%) = number (percentage) of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s): Seroconversion factors (SCF) for HI antibody titer at Day 21 (ATP cohort for immunogenicity HI)

Vaccine strain	Sub-group	Group	N	SCF		
				Value	95% CI	
					LL	UL
A/Solomon Islands	65-74y	Flu-1	253	11.9	10.1	14.0
		Flu-2	269	6.1	5.3	7.2
	75y+	Flu-1	192	7.6	6.3	9.1
		Flu-2	192	3.7	3.1	4.3
	65y+	Flu-1	445	9.8	8.7	11.1
		Flu-2	461	5.0	4.4	5.5
	18-40y	Flu-2	270	2.9	2.5	3.4
A/Wisconsin	65-74y	Flu-1	253	4.3	3.7	4.9
		Flu-2	269	2.8	2.5	3.1
	75y+	Flu-1	192	3.5	3.0	4.1
		Flu-2	192	2.7	2.4	3.1
	65y+	Flu-1	445	3.9	3.5	4.3
		Flu-2	461	2.7	2.5	3.0
	18-40y	Flu-2	270	2.2	2.0	2.5
B/Malaysia	65-74y	Flu-1	253	2.3	2.1	2.5
		Flu-2	269	1.8	1.7	2.0
	75y+	Flu-1	192	1.9	1.8	2.1
		Flu-2	192	1.9	1.7	2.1
	65y+	Flu-1	445	2.1	2.0	2.3
		Flu-2	461	1.8	1.7	2.0
	18-40y	Flu-2	270	1.9	1.7	2.1

N = number of subjects with pre- and post-vaccination results available
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable(s): Seroprotection rates (SPR) for HI antibody titer at Days 0 and 21 (ATP cohort for immunogenicity HI)

Vaccine strain	Sub-group	Group	Timing	N	SPR			
					n	%	95% CI	
							LL	UL
A/Solomon Islands	65-74y	Flu-1	PRE	253	43	17.0	12.6	22.2
			PI(D21)	255	229	89.8	85.4	93.2
		Flu-2	PRE	269	47	17.5	13.1	22.5
			PI(D21)	269	204	75.8	70.3	80.8
	75y+	Flu-1	PRE	192	28	14.6	9.9	20.4
			PI(D21)	192	152	79.2	72.7	84.7
		Flu-2	PRE	192	26	13.5	9.0	19.2
			PI(D21)	192	102	53.1	45.8	60.3
	65y+	Flu-1	PRE	445	71	16.0	12.7	19.7
			PI(D21)	447	381	85.2	81.6	88.4
		Flu-2	PRE	461	73	15.8	12.6	19.5
			PI(D21)	461	306	66.4	61.9	70.7
	18-40y	Flu-2	PRE	270	164	60.7	54.6	66.6
			PI(D21)	271	255	94.1	90.6	96.6
A/Wisconsin	65-74y	Flu-1	PRE	253	216	85.4	80.4	89.5
			PI(D21)	255	254	99.6	97.8	100
		Flu-2	PRE	269	215	79.9	74.6	84.5
			PI(D21)	269	259	96.3	93.3	98.2
	75y+	Flu-1	PRE	192	165	85.9	80.2	90.5
			PI(D21)	192	191	99.5	97.1	100
		Flu-2	PRE	192	147	76.6	69.9	82.4
			PI(D21)	192	183	95.3	91.3	97.8
	65y+	Flu-1	PRE	445	381	85.6	82.0	88.7
			PI(D21)	447	445	99.6	98.4	99.9

		Flu-2	PRE	461	362	78.5	74.5	82.2
			PI(D21)	461	442	95.9	93.6	97.5
	18-40y	Flu-2	PRE	270	235	87.0	82.4	90.8
			PI(D21)	271	270	99.6	98.0	100
B/Malaysia	65-74y	Flu-1	PRE	253	212	83.8	78.7	88.1
			PI(D21)	255	253	99.2	97.2	99.9
		Flu-2	PRE	269	232	86.2	81.5	90.1
			PI(D21)	269	256	95.2	91.9	97.4
	75y+	Flu-1	PRE	192	180	93.8	89.3	96.7
			PI(D21)	192	192	100	98.1	100
		Flu-2	PRE	192	167	87.0	81.4	91.4
			PI(D21)	192	187	97.4	94.0	99.1
	65y+	Flu-1	PRE	445	392	88.1	84.7	90.9
			PI(D21)	447	445	99.6	98.4	99.9
		Flu-2	PRE	461	399	86.6	83.1	89.5
			PI(D21)	461	443	96.1	93.9	97.7
	18-40y	Flu-2	PRE	270	236	87.4	82.8	91.1
			PI(D21)	271	268	98.9	96.8	99.8

N = number of subjects with available results
n (%) = number (percentage) of seroprotected subjects (HI titer ≥40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination (Day 0)
PI(D21) = Post-vaccination (Day 21)

Secondary Outcome Variable(s): Descriptive Statistics on the frequency of immune response marker-positive CD4 T-cells (per million CD4 T-cells) for pooled strains at Days 0 and 21 (ATP cohort for immunogenicity CMI)

Test description	Sub-group	Group	Timing	N	N miss	GM	SD	Median
CD4- All doubles	65-74y	Flu-1	PRE	35	3	1156.09	725.98	1094.00
			PI(D21)	38	0	1900.14	1224.62	1919.00
		Flu-2	PRE	36	0	779.33	534.62	800.00
			PI(D21)	36	0	888.86	789.66	961.50
	75y+	Flu-1	PRE	27	0	541.24	1080.77	1186.00
			PI(D21)	27	0	2184.02	1597.95	1971.00
		Flu-2	PRE	24	3	543.93	622.48	812.00
			PI(D21)	27	0	1198.21	1325.85	1560.00
	65y+	Flu-1	PRE	62	3	830.72	889.90	1098.50
			PI(D21)	65	0	2013.28	1388.55	1971.00
		Flu-2	PRE	60	3	674.91	567.07	812.00
			PI(D21)	63	0	1010.22	1069.96	1272.00
	18-40y	Flu-2	PRE	39	1	1276.25	701.42	1372.00
			PI(D21)	40	0	1607.66	839.45	1631.00
CD4-CD40L	65-74y	Flu-1	PRE	35	3	1146.24	710.31	1094.00
			PI(D21)	38	0	1844.34	1152.79	1900.00
		Flu-2	PRE	36	0	762.38	521.58	793.50
			PI(D21)	36	0	863.20	769.22	935.00
	75y+	Flu-1	PRE	27	0	534.72	1066.37	1153.00
			PI(D21)	27	0	2138.27	1563.28	1879.00
		Flu-2	PRE	24	3	531.64	624.95	782.00
			PI(D21)	27	0	1165.72	1316.76	1457.00
	65y+	Flu-1	PRE	62	3	822.37	875.39	1103.00
			PI(D21)	65	0	1961.18	1337.11	1879.00
		Flu-2	PRE	60	3	660.01	560.95	783.50
			PI(D21)	63	0	981.82	1056.18	1242.00
	18-40y	Flu-2	PRE	39	1	1260.65	681.46	1394.00
			PI(D21)	40	0	1556.00	830.54	1604.00
CD4-IFNγ	65-74y	Flu-1	PRE	35	3	575.41	510.90	578.00

			PI(D21)	38	0	1028.64	774.35	1133.50
		Flu-2	PRE	36	0	376.48	356.59	423.00
			PI(D21)	36	0	515.21	513.30	512.50
	75y+	Flu-1	PRE	27	0	442.56	682.65	660.00
			PI(D21)	27	0	1159.53	1188.22	1074.00
		Flu-2	PRE	24	3	364.50	452.17	549.50
			PI(D21)	27	0	663.69	840.10	714.00
	65y+	Flu-1	PRE	62	3	513.25	586.78	595.00
			PI(D21)	65	0	1081.11	966.36	1130.00
		Flu-2	PRE	60	3	371.64	397.45	463.00
			PI(D21)	63	0	574.28	685.03	653.00
	18-40y	Flu-2	PRE	39	1	753.45	556.25	697.00
			PI(D21)	40	0	870.84	589.37	839.00
CD4-IL2	65-74y	Flu-1	PRE	35	3	1016.46	632.66	953.00
			PI(D21)	38	0	1521.94	1002.05	1570.00
		Flu-2	PRE	36	0	693.00	462.46	701.00
			PI(D21)	36	0	755.18	672.46	845.50
	75y+	Flu-1	PRE	27	0	537.17	1007.12	1050.00
			PI(D21)	27	0	1833.46	1242.88	1635.00
		Flu-2	PRE	24	3	556.03	599.60	689.00
			PI(D21)	27	0	1013.34	1025.20	1314.00
	65y+	Flu-1	PRE	62	3	769.96	809.58	959.50
			PI(D21)	65	0	1644.34	1110.14	1577.00
		Flu-2	PRE	60	3	634.57	518.17	697.00
			PI(D21)	63	0	856.60	855.82	1060.00
	18-40y	Flu-2	PRE	39	1	1030.23	585.91	1038.00
			PI(D21)	40	0	1288.54	664.82	1191.00
CD4- TNFα	65-74y	Flu-1	PRE	35	3	760.83	601.91	692.00
			PI(D21)	38	0	1112.37	906.41	1198.50
		Flu-2	PRE	36	0	439.91	404.87	503.00
			PI(D21)	36	0	538.87	541.20	659.00
	75y+	Flu-1	PRE	27	0	418.38	819.23	745.00
			PI(D21)	27	0	1306.79	1007.16	1192.00
		Flu-2	PRE	24	3	366.76	439.43	547.50
			PI(D21)	27	0	715.54	853.77	938.00
	65y+	Flu-1	PRE	62	3	586.39	698.83	702.00
			PI(D21)	65	0	1189.34	945.05	1192.00
		Flu-2	PRE	60	3	409.05	415.62	539.00
			PI(D21)	63	0	608.51	700.32	720.00
	18-40y	Flu-2	PRE	39	1	746.02	551.82	820.00
			PI(D21)	40	0	921.15	549.61	995.00

All doubles: T-cells producing at least 2 cytokines
N = number of subjects with available results
N miss = number of subjects with missing results
GM = Geometric Mean
SD = Standard Deviation
PRE = Pre-vaccination (Day 0)
PI(D21) = Post-vaccination (Day 21)

Secondary Outcome Variable(s): Descriptive Statistics on the frequency of cytokine-positive CD4 T-cells (per million CD4 T-cells) for each strain at Days 0 and 21 (ATP cohort for immunogenicity CMI)

Test description	Vaccine strain	Sub-group	Group	Timing	N	N miss	GM	SD	Median
CD4- All doubles	A/Solomon Islands	65-74y	Flu-1	PRE	35	3	414.66	330.08	426.00
				PI(D21)	38	0	718.10	654.78	706.50
			Flu-2	PRE	36	0	195.43	305.29	335.00
				PI(D21)	36	0	267.22	406.15	355.50
		75y+	Flu-1	PRE	27	0	295.05	581.00	373.00

				PI(D21)	27	0	932.35	1411.97	806.00
			Flu-2	PRE	24	3	202.14	332.31	324.00
				PI(D21)	27	0	354.22	634.89	447.00
		65y+	Flu-1	PRE	62	3	357.55	452.52	411.50
				PI(D21)	65	0	800.36	1041.50	784.00
			Flu-2	PRE	60	3	198.09	314.56	324.00
				PI(D21)	63	0	301.53	523.52	371.00
		18-40y	Flu-2	PRE	39	1	447.08	355.07	458.00
				PI(D21)	40	0	610.52	403.34	645.00
	A/Wisconsin	65-74y	Flu-1	PRE	35	3	731.61	517.94	752.00
				PI(D21)	38	0	1094.75	755.76	1111.00
			Flu-2	PRE	36	0	550.74	377.21	622.50
				PI(D21)	36	0	536.01	418.21	696.50
		75y+	Flu-1	PRE	27	0	443.76	879.46	796.00
				PI(D21)	27	0	1192.24	1079.64	1138.00
			Flu-2	PRE	24	3	429.38	528.02	644.50
				PI(D21)	27	0	784.79	978.91	930.00
		65y+	Flu-1	PRE	62	3	588.47	692.26	768.00
				PI(D21)	65	0	1134.24	898.14	1138.00
			Flu-2	PRE	60	3	498.54	440.24	625.50
				PI(D21)	63	0	631.16	733.94	792.00
		18-40y	Flu-2	PRE	39	1	792.05	526.89	815.00
				PI(D21)	40	0	909.54	567.16	863.00
	B/Malaysia	65-74y	Flu-1	PRE	35	3	430.01	490.52	551.00
				PI(D21)	38	0	901.81	610.45	971.00
			Flu-2	PRE	36	0	307.41	302.59	345.00
				PI(D21)	36	0	351.22	419.99	420.50
		75y+	Flu-1	PRE	27	0	293.77	429.25	552.00
				PI(D21)	27	0	1064.71	1152.24	984.00
			Flu-2	PRE	24	3	301.94	416.99	477.00
				PI(D21)	27	0	364.50	961.01	785.00
		65y+	Flu-1	PRE	62	3	364.27	461.17	551.50
				PI(D21)	65	0	966.21	880.89	971.00
			Flu-2	PRE	60	3	305.21	353.99	381.00
				PI(D21)	63	0	356.85	718.07	493.00
		18-40y	Flu-2	PRE	39	1	682.52	421.14	660.00
				PI(D21)	40	0	955.56	436.64	1054.50
CD4-CD40L	A/Solomon Islands	65-74y	Flu-1	PRE	35	3	400.34	305.62	444.00
				PI(D21)	38	0	691.64	615.87	709.00
			Flu-2	PRE	36	0	183.43	290.31	285.00
				PI(D21)	36	0	254.22	395.64	313.00
		75y+	Flu-1	PRE	27	0	249.00	574.19	337.00
				PI(D21)	27	0	908.54	1375.45	758.00
			Flu-2	PRE	24	3	175.79	328.42	311.00
				PI(D21)	27	0	318.34	636.33	426.00
		65y+	Flu-1	PRE	62	3	325.56	439.08	411.50
				PI(D21)	65	0	774.62	1007.25	747.00
			Flu-2	PRE	60	3	180.33	304.08	299.00
				PI(D21)	63	0	279.94	518.71	365.00
		18-40y	Flu-2	PRE	39	1	440.15	347.16	458.00
				PI(D21)	40	0	583.10	386.83	635.00
	A/Wisconsin	65-74y	Flu-1	PRE	35	3	710.01	508.69	771.00

				PI(D21)	38	0	1061.14	712.50	1095.00
			Flu-2	PRE	36	0	536.85	362.80	621.50
				PI(D21)	36	0	470.23	406.77	678.00
		75y+	Flu-1	PRE	27	0	441.10	862.07	767.00
				PI(D21)	27	0	1164.43	1050.26	1078.00
			Flu-2	PRE	24	3	417.23	522.33	646.00
				PI(D21)	27	0	775.65	974.27	911.00
		65y+	Flu-1	PRE	62	3	577.08	678.98	769.00
				PI(D21)	65	0	1102.88	863.08	1078.00
			Flu-2	PRE	60	3	485.35	430.29	622.50
				PI(D21)	63	0	582.72	729.68	771.00
		18-40y	Flu-2	PRE	39	1	764.17	507.65	778.00
				PI(D21)	40	0	863.63	552.86	824.00
	B/Malaysia	65-74y	Flu-1	PRE	35	3	431.01	473.08	537.00
				PI(D21)	38	0	886.23	578.84	887.00
			Flu-2	PRE	36	0	299.61	296.87	345.00
				PI(D21)	36	0	334.92	411.97	412.00
		75y+	Flu-1	PRE	27	0	289.65	423.31	553.00
				PI(D21)	27	0	1070.45	1108.62	984.00
			Flu-2	PRE	24	3	295.71	413.47	458.00
				PI(D21)	27	0	367.70	957.31	775.00
		65y+	Flu-1	PRE	62	3	362.51	448.54	545.00
				PI(D21)	65	0	958.56	845.72	969.00
			Flu-2	PRE	60	3	298.05	349.21	391.00
				PI(D21)	63	0	348.60	713.03	470.00
		18-40y	Flu-2	PRE	39	1	683.48	402.08	660.00
				PI(D21)	40	0	922.93	427.46	1016.00
CD4-IFNγ	A/Solomon Islands	65-74y	Flu-1	PRE	35	3	212.48	208.50	304.00
				PI(D21)	38	0	385.92	406.56	379.50
			Flu-2	PRE	36	0	155.71	223.85	182.00
				PI(D21)	36	0	191.22	252.80	195.50
		75y+	Flu-1	PRE	27	0	149.56	318.20	217.00
				PI(D21)	27	0	522.76	810.52	489.00
			Flu-2	PRE	24	3	91.30	252.99	215.50
				PI(D21)	27	0	264.37	479.08	239.00
		65y+	Flu-1	PRE	62	3	182.35	259.80	244.00
				PI(D21)	65	0	437.77	612.28	436.00
			Flu-2	PRE	60	3	125.77	233.84	198.50
				PI(D21)	63	0	219.70	371.51	206.00
		18-40y	Flu-2	PRE	39	1	278.48	252.29	273.00
				PI(D21)	40	0	359.22	287.60	332.00
	A/Wisconsin	65-74y	Flu-1	PRE	35	3	351.41	313.36	359.00
				PI(D21)	38	0	573.71	468.21	629.50
			Flu-2	PRE	36	0	207.40	244.54	331.50
				PI(D21)	36	0	270.09	245.47	321.00
		75y+	Flu-1	PRE	27	0	242.52	600.09	378.00
				PI(D21)	27	0	633.88	740.07	566.00
			Flu-2	PRE	24	3	287.67	381.85	350.00
				PI(D21)	27	0	381.80	722.02	438.00
		65y+	Flu-1	PRE	62	3	299.00	456.69	368.50
				PI(D21)	65	0	597.98	592.41	608.00
			Flu-2	PRE	60	3	236.40	307.12	346.00

				PI(D21)	63	0	313.28	520.59	357.00
		18-40y	Flu-2	PRE	39	1	363.65	347.00	350.00
				PI(D21)	40	0	418.05	342.88	381.50
	B/Malaysia	65-74y	Flu-1	PRE	35	3	199.20	331.85	288.00
				PI(D21)	38	0	495.57	432.71	493.00
			Flu-2	PRE	36	0	142.07	186.37	172.50
				PI(D21)	36	0	198.67	255.19	179.50
		75y+	Flu-1	PRE	27	0	193.93	329.77	287.00
				PI(D21)	27	0	487.84	753.29	584.00
			Flu-2	PRE	24	3	186.69	289.66	218.50
				PI(D21)	27	0	308.51	670.47	369.00
		65y+	Flu-1	PRE	62	3	196.89	328.87	287.50
				PI(D21)	65	0	492.35	589.63	561.00
			Flu-2	PRE	60	3	158.47	236.31	200.00
				PI(D21)	63	0	239.91	488.70	270.00
		18-40y	Flu-2	PRE	39	1	403.93	337.61	409.00
				PI(D21)	40	0	569.37	334.37	567.50
CD4-IL2	A/Solomon Islands	65-74y	Flu-1	PRE	35	3	369.01	272.23	399.00
				PI(D21)	38	0	562.99	447.30	602.00
			Flu-2	PRE	36	0	208.40	270.29	252.50
				PI(D21)	36	0	241.55	351.02	312.50
		75y+	Flu-1	PRE	27	0	229.16	521.85	310.00
				PI(D21)	27	0	790.57	1127.38	660.00
			Flu-2	PRE	24	3	160.54	307.85	321.50
				PI(D21)	27	0	281.96	504.30	417.00
		65y+	Flu-1	PRE	62	3	299.87	397.15	362.50
				PI(D21)	65	0	648.25	811.35	632.00
			Flu-2	PRE	60	3	187.75	284.65	272.00
				PI(D21)	63	0	258.10	426.17	354.00
		18-40y	Flu-2	PRE	39	1	407.21	294.28	436.00
				PI(D21)	40	0	497.37	341.43	546.00
	A/Wisconsin	65-74y	Flu-1	PRE	35	3	631.50	442.57	636.00
				PI(D21)	38	0	849.48	553.92	889.50
			Flu-2	PRE	36	0	464.97	349.29	544.00
				PI(D21)	36	0	471.28	345.03	589.50
		75y+	Flu-1	PRE	27	0	384.00	826.94	693.00
				PI(D21)	27	0	976.15	883.07	850.00
			Flu-2	PRE	24	3	385.81	486.74	535.00
				PI(D21)	27	0	692.80	839.39	738.00
		65y+	Flu-1	PRE	62	3	508.50	633.33	642.00
				PI(D21)	65	0	899.97	707.01	887.00
			Flu-2	PRE	60	3	431.52	406.74	537.00
				PI(D21)	63	0	555.89	627.06	664.00
		18-40y	Flu-2	PRE	39	1	625.28	419.87	683.00
				PI(D21)	40	0	683.81	486.05	660.00
	B/Malaysia	65-74y	Flu-1	PRE	35	3	426.22	417.29	481.00
				PI(D21)	38	0	758.18	495.44	822.00
			Flu-2	PRE	36	0	319.95	279.14	334.00
				PI(D21)	36	0	313.88	392.97	399.00
		75y+	Flu-1	PRE	27	0	260.57	422.63	504.00
				PI(D21)	27	0	992.76	968.06	889.00
			Flu-2	PRE	24	3	316.28	422.57	418.00
				PI(D21)	27	0	430.70	721.00	646.00
		65y+	Flu-1	PRE	62	3	344.01	416.21	492.50
				PI(D21)	65	0	848.01	741.60	870.00
			Flu-2	PRE	60	3	318.48	344.45	354.00

				PI(D21)	63	0	359.46	568.15	437.00
		18-40y	Flu-2	PRE	39	1	591.42	369.78	604.00
				PI(D21)	40	0	816.79	387.12	848.50
CD4- TNFα	A/Solomon Islands	65-74y	Flu-1	PRE	35	3	233.90	255.09	294.00
				PI(D21)	38	0	364.50	497.37	471.50
			Flu-2	PRE	36	0	82.31	223.47	216.50
				PI(D21)	36	0	120.23	307.75	182.50
		75y+	Flu-1	PRE	27	0	156.09	467.04	222.00
				PI(D21)	27	0	490.23	926.69	444.00
			Flu-2	PRE	24	3	116.84	263.15	183.00
				PI(D21)	27	0	195.80	435.66	257.00
		65y+	Flu-1	PRE	62	3	196.12	360.16	275.50
				PI(D21)	65	0	412.25	706.12	450.00
			Flu-2	PRE	60	3	94.69	238.17	191.50
				PI(D21)	63	0	148.17	369.80	221.00
		18-40y	Flu-2	PRE	39	1	231.87	253.92	356.00
				PI(D21)	40	0	280.36	260.15	385.00
	A/Wisconsin	65-74y	Flu-1	PRE	35	3	535.50	405.19	542.00
				PI(D21)	38	0	719.50	563.34	741.50
			Flu-2	PRE	36	0	341.35	325.22	467.50
				PI(D21)	36	0	414.31	308.40	432.50
		75y+	Flu-1	PRE	27	0	307.24	741.25	575.00
				PI(D21)	27	0	809.46	679.34	745.00
			Flu-2	PRE	24	3	316.70	435.99	404.50
				PI(D21)	27	0	511.80	579.94	613.00
		65y+	Flu-1	PRE	62	3	420.42	570.76	558.50
				PI(D21)	65	0	755.59	609.80	745.00
			Flu-2	PRE	60	3	331.27	370.01	436.00
				PI(D21)	63	0	453.58	458.72	475.00
		18-40y	Flu-2	PRE	39	1	506.31	425.15	562.00
				PI(D21)	40	0	591.75	404.06	549.50
	B/Malaysia	65-74y	Flu-1	PRE	35	3	193.73	367.36	296.00
				PI(D21)	38	0	433.46	406.30	495.50
			Flu-2	PRE	36	0	101.98	183.84	157.50
				PI(D21)	36	0	118.32	214.89	179.00
		75y+	Flu-1	PRE	27	0	144.76	316.58	296.00
				PI(D21)	27	0	495.29	691.58	468.00
			Flu-2	PRE	24	3	156.00	226.12	284.50
				PI(D21)	27	0	172.12	636.84	369.00
		65y+	Flu-1	PRE	62	3	170.64	343.45	296.00
				PI(D21)	65	0	458.14	542.16	488.00
			Flu-2	PRE	60	3	120.88	202.77	235.50
				PI(D21)	63	0	138.94	460.35	228.00
		18-40y	Flu-2	PRE	39	1	351.20	284.54	423.00
				PI(D21)	40	0	480.87	289.81	515.00

All doubles: T-cells producing at least 2 cytokines
N = number of subjects with available results
N miss = number of subjects with missing results
GM = Geometric Mean
SD = Standard Deviation
PRE = Pre-vaccination (Day 0)
PI(D21) = Post-vaccination (Day 21)

Secondary Outcome Variable(s): Descriptive Statistics on the frequency of cytokine-positive CD8 T-cells (per million CD8 T-cells) for pooled strains at Days 0 and 21 (ATP cohort for immunogenicity CMI)								
Test description	**Sub-group**	**Group**	**Timing**	**N**	**N miss**	**GM**	**SD**	**Median**
CD8- All doubles	65-74y	Flu-1	PRE	34	4	4.76	52.40	1.00
			PI(D21)	38	0	13.28	138.04	47.00
		Flu-2	PRE	34	2	9.91	147.48	3.50
			PI(D21)	36	0	9.51	118.67	1.00
	75y+	Flu-1	PRE	21	6	20.08	247.84	75.00
			PI(D21)	26	1	23.50	204.36	82.50
		Flu-2	PRE	20	7	3.62	48.23	1.00
			PI(D21)	26	1	3.85	101.22	1.00
	65y+	Flu-1	PRE	55	10	8.25	166.35	1.00
			PI(D21)	64	1	16.75	168.54	76.50
		Flu-2	PRE	54	9	6.82	123.10	1.00
			PI(D21)	62	1	6.51	112.42	1.00
	18-40y	Flu-2	PRE	39	1	3.56	247.08	1.00
			PI(D21)	40	0	3.48	79.78	1.00
CD8-CD40L	65-74y	Flu-1	PRE	34	4	3.92	47.52	1.00
			PI(D21)	38	0	5.53	125.01	1.00
		Flu-2	PRE	34	2	5.20	162.59	1.00
			PI(D21)	36	0	7.18	83.96	1.00
	75y+	Flu-1	PRE	21	6	13.00	179.18	4.00
			PI(D21)	26	1	14.12	123.08	75.50
		Flu-2	PRE	20	7	3.17	56.44	1.00
			PI(D21)	26	1	4.29	87.06	1.00
	65y+	Flu-1	PRE	55	10	6.19	120.88	1.00
			PI(D21)	64	1	8.09	123.89	1.00
		Flu-2	PRE	54	9	4.33	134.18	1.00
			PI(D21)	62	1	5.79	85.20	1.00
	18-40y	Flu-2	PRE	39	1	2.12	220.32	1.00
			PI(D21)	40	0	3.64	71.55	1.00
CD8- IFNγ	65-74y	Flu-1	PRE	34	4	2.87	38.73	1.00
			PI(D21)	38	0	2.30	38.65	1.00
		Flu-2	PRE	34	2	3.46	55.33	1.00
			PI(D21)	36	0	3.74	68.11	1.00
	75y+	Flu-1	PRE	21	6	2.61	102.64	1.00
			PI(D21)	26	1	4.76	143.13	1.00
		Flu-2	PRE	20	7	1.66	40.19	1.00
			PI(D21)	26	1	1.92	28.56	1.00
	65y+	Flu-1	PRE	55	10	2.77	69.92	1.00
			PI(D21)	64	1	3.09	97.36	1.00
		Flu-2	PRE	54	9	2.64	50.62	1.00
			PI(D21)	62	1	2.82	56.06	1.00
	18-40y	Flu-2	PRE	39	1	1.58	32.08	1.00
			PI(D21)	40	0	2.17	28.97	1.00
CD8-IL2	65-74y	Flu-1	PRE	34	4	2.91	40.28	1.00
			PI(D21)	38	0	9.43	148.31	1.50
		Flu-2	PRE	34	2	12.49	142.53	71.00
			PI(D21)	36	0	8.31	109.45	1.00
	75y+	Flu-1	PRE	21	6	27.13	195.86	75.00
			PI(D21)	26	1	19.62	173.95	79.50
		Flu-2	PRE	20	7	4.32	56.67	1.00
			PI(D21)	26	1	3.29	87.12	1.00
	65y+	Flu-1	PRE	55	10	6.82	135.79	1.00
			PI(D21)	64	1	12.70	159.08	12.50
		Flu-2	PRE	54	9	8.43	119.70	1.00

			PI(D21)	62	1	5.64	101.15	1.00
	18-40y	Flu-2	PRE	39	1	3.21	249.46	1.00
			PI(D21)	40	0	3.20	55.75	1.00
CD8- TNFα	65-74y	Flu-1	PRE	34	4	2.22	37.61	1.00
			PI(D21)	38	0	6.40	73.30	1.00
		Flu-2	PRE	34	2	2.69	49.02	1.00
			PI(D21)	36	0	3.43	73.31	1.00
	75y+	Flu-1	PRE	21	6	5.09	104.51	1.00
			PI(D21)	26	1	4.75	109.85	1.00
		Flu-2	PRE	20	7	2.16	28.17	1.00
			PI(D21)	26	1	3.69	65.83	1.00
	65y+	Flu-1	PRE	55	10	3.05	72.38	1.00
			PI(D21)	64	1	5.67	89.23	1.00
		Flu-2	PRE	54	9	2.48	42.55	1.00
			PI(D21)	62	1	3.54	69.71	1.00
	18-40y	Flu-2	PRE	39	1	3.13	44.03	1.00
			PI(D21)	40	0	2.73	40.30	1.00

All doubles: T-cells producing at least 2 cytokines
N = number of subjects with available results
N miss = number of subjects with missing results
GM= Geometric Mean
SD = Standard Deviation
PRE = Pre-vaccination (Day 0)
PI(D21) = Post-vaccination (Day 21)

Secondary Outcome Variable(s): Descriptive Statistics on the frequency of cytokine-positive CD8 T-cells (per million CD8 T-cells) for each strain at Days 0 and 21 (ATP cohort for immunogenicity CMI)

Test description	Vaccine strain	Sub-group	Group	Timing	N	N miss	GM	SD	Median
CD8- All doubles	A/Solomon Islands	65-74y	Flu-1	PRE	35	3	1.68	33.86	1.00
				PI(D21)	38	0	2.35	45.59	1.00
			Flu-2	PRE	35	1	2.38	30.40	1.00
				PI(D21)	36	0	2.16	36.62	1.00
		75y+	Flu-1	PRE	26	1	1.91	115.52	1.00
				PI(D21)	27	0	3.34	116.29	1.00
			Flu-2	PRE	23	4	1.99	53.20	1.00
				PI(D21)	26	1	2.98	53.89	1.00
		65y+	Flu-1	PRE	61	4	1.78	79.34	1.00
				PI(D21)	65	0	2.72	83.49	1.00
			Flu-2	PRE	58	5	2.21	40.56	1.00
				PI(D21)	62	1	2.47	44.67	1.00
		18-40y	Flu-2	PRE	39	1	1.74	24.59	1.00
				PI(D21)	40	0	1.77	37.02	1.00
	A/Wisconsin	65-74y	Flu-1	PRE	35	3	3.92	90.62	1.00
				PI(D21)	38	0	7.40	86.29	1.00
			Flu-2	PRE	35	1	3.39	115.56	1.00
				PI(D21)	36	0	2.84	117.27	1.00
		75y+	Flu-1	PRE	26	1	4.33	257.10	1.00
				PI(D21)	27	0	4.05	120.17	1.00
			Flu-2	PRE	22	5	4.11	53.27	1.00
				PI(D21)	26	1	4.38	63.35	1.00
		65y+	Flu-1	PRE	61	4	4.09	180.98	1.00
				PI(D21)	65	0	5.76	100.86	1.00
			Flu-2	PRE	57	6	3.65	96.03	1.00
				PI(D21)	62	1	3.41	97.74	1.00
		18-40y	Flu-2	PRE	39	1	2.94	54.51	1.00
				PI(D21)	40	0	2.28	57.61	1.00

	B/Malaysia	65-74y	Flu-1	PRE	34	4	4.70	81.42	1.00
				PI(D21)	38	0	5.46	53.91	1.00
			Flu-2	PRE	34	2	4.16	71.35	1.00
				PI(D21)	36	0	3.69	52.69	1.00
		75y+	Flu-1	PRE	22	5	5.04	82.23	1.00
				PI(D21)	27	0	2.07	90.52	1.00
			Flu-2	PRE	21	6	4.35	101.79	1.00
				PI(D21)	25	2	2.33	29.86	1.00
		65y+	Flu-1	PRE	56	9	4.84	81.00	1.00
				PI(D21)	65	0	3.65	70.94	1.00
			Flu-2	PRE	55	8	4.23	83.53	1.00
				PI(D21)	61	2	3.06	44.91	1.00
		18-40y	Flu-2	PRE	39	1	4.46	67.12	1.00
				PI(D21)	40	0	2.25	29.06	1.00
CD8-CD40L	A/Solomon Islands	65-74y	Flu-1	PRE	35	3	1.48	31.29	1.00
				PI(D21)	38	0	2.05	37.71	1.00
			Flu-2	PRE	35	1	1.67	32.97	1.00
				PI(D21)	36	0	1.57	21.02	1.00
		75y+	Flu-1	PRE	26	1	1.74	48.32	1.00
				PI(D21)	27	0	1.50	72.48	1.00
			Flu-2	PRE	23	4	1.96	90.89	1.00
				PI(D21)	26	1	2.83	41.86	1.00
		65y+	Flu-1	PRE	61	4	1.59	39.18	1.00
				PI(D21)	65	0	1.80	54.38	1.00
			Flu-2	PRE	58	5	1.78	62.52	1.00
				PI(D21)	62	1	2.01	32.04	1.00
		18-40y	Flu-2	PRE	39	1	1.27	26.87	1.00
				PI(D21)	40	0	1.71	24.13	1.00
	A/Wisconsin	65-74y	Flu-1	PRE	35	3	2.41	59.31	1.00
				PI(D21)	38	0	4.53	81.34	1.00
			Flu-2	PRE	35	1	3.43	66.94	1.00
				PI(D21)	36	0	2.11	73.64	1.00
		75y+	Flu-1	PRE	26	1	4.38	170.93	1.00
				PI(D21)	27	0	4.25	103.75	1.00
			Flu-2	PRE	22	5	4.28	75.14	1.00
				PI(D21)	26	1	4.69	56.42	1.00
		65y+	Flu-1	PRE	61	4	3.11	121.55	1.00
				PI(D21)	65	0	4.41	90.57	1.00
			Flu-2	PRE	57	6	3.74	69.67	1.00
				PI(D21)	62	1	2.95	66.69	1.00
		18-40y	Flu-2	PRE	39	1	3.08	37.81	1.00
				PI(D21)	40	0	1.64	42.73	1.00
	B/Malaysia	65-74y	Flu-1	PRE	34	4	3.81	63.78	1.00
				PI(D21)	38	0	3.83	40.57	1.00
			Flu-2	PRE	34	2	4.19	89.78	1.00
				PI(D21)	36	0	2.34	46.19	1.00
		75y+	Flu-1	PRE	22	5	3.92	75.68	1.00
				PI(D21)	27	0	1.75	45.53	1.00
			Flu-2	PRE	21	6	3.46	89.61	1.00
				PI(D21)	25	2	2.80	32.88	1.00
		65y+	Flu-1	PRE	56	9	3.85	68.08	1.00
				PI(D21)	65	0	2.76	42.53	1.00
			Flu-2	PRE	55	8	3.90	88.91	1.00
				PI(D21)	61	2	2.52	40.95	1.00
		18-40y	Flu-2	PRE	39	1	3.24	57.80	1.00
				PI(D21)	40	0	2.12	27.99	1.00

CD8-IFNγ	A/Solomon Islands	65-74y	Flu-1	PRE	35	3	1.65	25.31	1.00
				PI(D21)	38	0	1.41	20.63	1.00
			Flu-2	PRE	35	1	1.13	12.17	1.00
				PI(D21)	36	0	1.69	25.42	1.00
		75y+	Flu-1	PRE	26	1	2.18	117.73	1.00
				PI(D21)	27	0	2.60	98.26	1.00
			Flu-2	PRE	23	4	2.14	30.24	1.00
				PI(D21)	26	1	1.46	47.44	1.00
		65y+	Flu-1	PRE	61	4	1.86	79.40	1.00
				PI(D21)	65	0	1.82	66.62	1.00
			Flu-2	PRE	58	5	1.46	21.76	1.00
				PI(D21)	62	1	1.59	35.99	1.00
		18-40y	Flu-2	PRE	39	1	1.27	25.94	1.00
				PI(D21)	40	0	1.76	40.44	1.00
	A/Wisconsin	65-74y	Flu-1	PRE	35	3	1.95	29.24	1.00
				PI(D21)	38	0	2.24	30.93	1.00
			Flu-2	PRE	35	1	1.78	66.10	1.00
				PI(D21)	36	0	1.88	40.00	1.00
		75y+	Flu-1	PRE	26	1	2.04	49.00	1.00
				PI(D21)	27	0	2.03	55.28	1.00
			Flu-2	PRE	22	5	2.11	27.23	1.00
				PI(D21)	26	1	1.74	27.73	1.00
		65y+	Flu-1	PRE	61	4	1.99	38.64	1.00
				PI(D21)	65	0	2.15	42.44	1.00
			Flu-2	PRE	57	6	1.90	54.31	1.00
				PI(D21)	62	1	1.82	35.19	1.00
		18-40y	Flu-2	PRE	39	1	1.77	31.47	1.00
				PI(D21)	40	0	1.94	33.33	1.00
	B/Malaysia	65-74y	Flu-1	PRE	34	4	1.82	63.31	1.00
				PI(D21)	38	0	1.64	45.20	1.00
			Flu-2	PRE	34	2	1.72	35.25	1.00
				PI(D21)	36	0	1.67	42.12	1.00
		75y+	Flu-1	PRE	22	5	2.37	40.84	1.00
				PI(D21)	27	0	2.43	72.98	1.00
			Flu-2	PRE	21	6	1.90	32.37	1.00
				PI(D21)	25	2	1.33	16.52	1.00
		65y+	Flu-1	PRE	56	9	2.02	55.17	1.00
				PI(D21)	65	0	1.93	58.24	1.00
			Flu-2	PRE	55	8	1.78	33.87	1.00
				PI(D21)	61	2	1.52	34.11	1.00
		18-40y	Flu-2	PRE	39	1	1.98	27.33	1.00
				PI(D21)	40	0	1.55	24.38	1.00
CD8-IL2	A/Solomon Islands	65-74y	Flu-1	PRE	35	3	2.16	37.07	1.00
				PI(D21)	38	0	2.37	46.94	1.00
			Flu-2	PRE	35	1	2.39	30.97	1.00
				PI(D21)	36	0	2.12	36.46	1.00
		75y+	Flu-1	PRE	26	1	1.42	25.65	1.00
				PI(D21)	27	0	3.15	103.34	1.00
			Flu-2	PRE	23	4	1.90	54.48	1.00
				PI(D21)	26	1	2.95	58.14	1.00
		65y+	Flu-1	PRE	61	4	1.80	32.72	1.00
				PI(D21)	65	0	2.66	75.77	1.00
			Flu-2	PRE	58	5	2.18	41.49	1.00
				PI(D21)	62	1	2.43	46.74	1.00
		18-40y	Flu-2	PRE	39	1	1.55	22.29	1.00
				PI(D21)	40	0	1.97	38.08	1.00

	A/Wisconsin	65-74y	Flu-1	PRE	35	3	3.45	83.28	1.00
				PI(D21)	38	0	6.04	89.40	1.00
			Flu-2	PRE	35	1	3.93	111.38	1.00
				PI(D21)	36	0	2.78	88.92	1.00
		75y+	Flu-1	PRE	26	1	4.33	257.10	1.00
				PI(D21)	27	0	4.70	109.57	1.00
			Flu-2	PRE	22	5	4.17	51.02	1.00
				PI(D21)	26	1	6.03	55.32	1.00
		65y+	Flu-1	PRE	61	4	3.80	179.33	1.00
				PI(D21)	65	0	5.44	97.47	1.00
			Flu-2	PRE	57	6	4.02	92.65	1.00
				PI(D21)	62	1	3.85	76.13	1.00
		18-40y	Flu-2	PRE	39	1	2.84	48.01	1.00
				PI(D21)	40	0	2.47	61.35	1.00
	B/Malaysia	65-74y	Flu-1	PRE	34	4	4.15	70.14	1.00
				PI(D21)	38	0	4.98	40.20	1.00
			Flu-2	PRE	34	2	4.76	71.18	1.00
				PI(D21)	36	0	3.16	40.90	1.00
		75y+	Flu-1	PRE	22	5	3.36	97.69	1.00
				PI(D21)	27	0	2.36	91.00	1.00
			Flu-2	PRE	21	6	4.41	89.45	1.00
				PI(D21)	25	2	2.20	25.81	1.00
		65y+	Flu-1	PRE	56	9	3.82	81.23	1.00
				PI(D21)	65	0	3.65	65.57	1.00
			Flu-2	PRE	55	8	4.62	77.91	1.00
				PI(D21)	61	2	2.73	35.72	1.00
		18-40y	Flu-2	PRE	39	1	3.21	52.63	1.00
				PI(D21)	40	0	1.94	32.16	1.00
CD8-TNFα	A/Solomon Islands	65-74y	Flu-1	PRE	35	3	2.12	30.36	1.00
				PI(D21)	38	0	1.78	27.40	1.00
			Flu-2	PRE	35	1	1.85	26.43	1.00
				PI(D21)	36	0	2.98	34.33	1.00
		75y+	Flu-1	PRE	26	1	2.71	80.20	1.00
				PI(D21)	27	0	3.78	112.57	1.00
			Flu-2	PRE	23	4	1.83	38.96	1.00
				PI(D21)	26	1	1.71	42.40	1.00
		65y+	Flu-1	PRE	61	4	2.35	57.09	1.00
				PI(D21)	65	0	2.43	77.68	1.00
			Flu-2	PRE	58	5	1.84	31.70	1.00
				PI(D21)	62	1	2.36	37.71	1.00
		18-40y	Flu-2	PRE	39	1	1.73	24.53	1.00
				PI(D21)	40	0	1.58	39.16	1.00
	A/Wisconsin	65-74y	Flu-1	PRE	35	3	2.48	76.34	1.00
				PI(D21)	38	0	3.52	44.37	1.00
			Flu-2	PRE	35	1	3.34	76.04	1.00
				PI(D21)	36	0	2.84	88.11	1.00
		75y+	Flu-1	PRE	26	1	2.26	138.63	1.00
				PI(D21)	27	0	3.44	64.14	1.00
			Flu-2	PRE	22	5	1.22	16.42	1.00
				PI(D21)	26	1	2.34	33.99	1.00
		65y+	Flu-1	PRE	61	4	2.38	106.57	1.00
				PI(D21)	65	0	3.49	53.15	1.00
			Flu-2	PRE	57	6	2.26	62.04	1.00
				PI(D21)	62	1	2.62	70.62	1.00
		18-40y	Flu-2	PRE	39	1	1.97	32.90	1.00
				PI(D21)	40	0	1.90	26.17	1.00

	B/Malaysia	65-74y	Flu-1	PRE	34	4	1.83	57.53	1.00
				PI(D21)	38	0	2.27	36.57	1.00
			Flu-2	PRE	34	2	1.16	14.57	1.00
				PI(D21)	36	0	2.15	41.28	1.00
		75y+	Flu-1	PRE	22	5	1.98	51.24	1.00
				PI(D21)	27	0	1.78	61.66	1.00
			Flu-2	PRE	21	6	2.33	34.94	1.00
				PI(D21)	25	2	1.27	15.99	1.00
		65y+	Flu-1	PRE	56	9	1.88	54.67	1.00
				PI(D21)	65	0	2.05	48.15	1.00
			Flu-2	PRE	55	8	1.52	25.05	1.00
				PI(D21)	61	2	1.74	33.82	1.00
		18-40y	Flu-2	PRE	39	1	1.85	43.98	1.00
				PI(D21)	40	0	1.63	23.61	1.00

All doubles: T-cells producing at least 2 cytokines
N = number of subjects with available results
N miss = number of subjects with missing results
GM= Geometric Mean
SD = Standard Deviation
PRE = Pre-vaccination (Day 0)
PI(D21) = Post-vaccination (Day 21)

Secondary Outcome Variable(s): Number (%) of subjects with unsolicited adverse events resulting in a medically attended visit within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated Cohort)

Most frequent adverse events resulting in a medically attended visit	**65y+**		**18-40y**
	Flu-1 Group N = 475	**Flu-2 Group N = 488**	**Flu-2 Group N = 289**
Subjects with any AE(s), n (%)	22 (4.6)	25 (5.1)	11 (3.8)
Subjects with grade 3* AE(s), n (%)	3 (0.6)	3 (0.6)	2 (0.7)
Subjects with related** AE(s), n (%)	1 (0.2)	1 (0.2)	1 (0.3)
Sinusitis	2 (0.4)	2 (0.4)	1 (0.3)
Upper respiratory tract infection	1 (0.2)	3 (0.6)	-
Viral Infection	1 (0.2)	-	2 (0.7)
Cystitis	1 (0.2)	2 (0.4)	1 (0.3)
Back pain	1 (0.2)	2 (0.4)	-
Bronchitis	1 (0.2)	1 (0.2)	1 (0.3)
Sciatica	1 (0.2)	1 (0.2)	-
Abscess oral	-	-	1 (0.3)
Acne	1 (0.2)	-	1 (0.3)
Ankle fracture	-	-	1 (0.3)
Tendonitis	1 (0.2)	-	1 (0.3)
Tooth abscess	1 (0.2)	-	1 (0.3)
Hypoaesthesia facial	-	-	1 (0.3)
Pharyngitis	-	-	1 (0.3)
Vaginal infection	-	-	1 (0.3)
Gastrooesophageal reflux disease	-	1 (0.2)	-
Nausea	-	1 (0.2)	-
Toothache	-	1 (0.2)	-
Chest pain	-	1 (0.2)	-
Influenza like illness	-	1 (0.2)	-
Injection site pain	1 (0.2)	-	-
Acute tonsillitis	-	1 (0.2)	-
Cellulitis	-	1 (0.2)	-
Gastroenteritis	1 (0.2)	-	-
Pneumonia	1 (0.2)	-	-
Urinary tract infection	-	3 (0.6)	-
Hand fracture	-	1 (0.2)	-

Head injury	1 (0.2)	-	-
Hip fracture	-	1 (0.2)	-
Open wound	-	1 (0.2)	-
Skin laceration	1 (0.2)	-	-
Ulna fracture	1 (0.2)	-	-
Blood pressure increased	1 (0.2)	-	-
Gout	1 (0.2)	-	-
Arthralgia	1 (0.2)	-	-
Bursitis	-	1 (0.2)	-
Intervertebral disc degeneration	-	1 (0.2)	-
Osteopenia	1 (0.2)	-	-
Dizziness	1 (0.2)	-	-
Productive cough	-	1 (0.2)	-
Hyperkeratosis	-	1 (0.2)	-
Psoriasis	1 (0.2)	-	-
Dental implantation	-	1 (0.2)	-

- : Adverse Event absent
* Grade 3 AE: AE that prevented normal activity
** Related AE: AE assessed by the investigator as causally related to the study vaccination

Secondary Outcome Variable(s): Number (%) of subjects with unsolicited AEs resulting in a medically attended visit during the long-term follow-up between Day 21 and Day 179 (Total Vaccinated Cohort)

Most frequent adverse events resulting in a medically attended visit	**65y+**		**18-40y**
	Flu-1 Group N = 475	**Flu-2 Group N = 488**	**Flu-2 Group N = 289**
Subjects with any AE(s), n (%)	112 (23.6)	137 (28.1)	71 (24.6)
Subjects with grade 3* AE(s), n (%)	23 (4.8)	29 (5.9)	20 (6.9)
Subjects with related** AE(s), n (%)	0 (0.0)	0 (0.0)	1 (0.3)
Upper respiratory tract infection	12 (2.5)	13 (2.7)	4 (1.4)
Bronchitis	9 (1.9)	9 (1.8)	6 (2.1)
Influenza like illness	5 (1.1)	3 (0.6)	6 (2.1)
Nasopharyngitis	2 (0.4)	4 (0.8)	7 (2.4)
Pneumonia	7 (1.5)	6 (1.2)	-
Cystitis	2 (0.4)	7 (1.4)	3 (1.0)
Back pain	4 (0.8)	3 (0.6)	4 (1.4)
Sinusitis	-	4 (0.8)	10 (3.5)
Cough	4 (0.8)	5 (1.0)	-
Hypertension	2 (0.4)	5 (1.0)	-
Tonsillitis	3 (0.6)	3 (0.6)	-
Gastroenteritis	-	-	5 (1.7)
Gastritis	2 (0.4)	3 (0.6)	-
Pharyngitis	-	-	4 (1.4)
Arthralgia	-	3 (0.6)	3 (1.0)
Contusion	-	-	3 (1.0)
Urinary tract infection	7 (1.5)	-	3 (1.0)
Dyspnoea	2 (0.4)	-	-
Gastrooesophageal reflux disease	2 (0.4)	-	-
Herpes zoster	4 (0.8)	-	-
Atrial fibrillation	-	3 (0.6)	-
Bursitis	-	3 (0.6)	-
Diabetes mellitus	-	3 (0.6)	-
Diarrhoea	-	3 (0.6)	-
Vertigo	-	3 (0.6)	-
Abdominal pain	2 (0.4)	-	-
Cataract	2 (0.4)	-	-
Chronic obstructive pulmonary disease	2 (0.4)	-	-
Dermatitis	2 (0.4)	-	-

Dizziness	2 (0.4)	-	-
Dry eye	2 (0.4)	-	-
Lichenoid keratosis	2 (0.4)	-	-
Pruritus	2 (0.4)	-	-
Radius fracture	2 (0.4)	-	-
Rash	2 (0.4)	-	-
Rib fracture	2 (0.4)	-	-
Scoliosis	2 (0.4)	-	-
Tooth abscess	2 (0.4)	-	-
Type 2 diabetes mellitus	2 (0.4)	-	-

Counting rule applied: As there were more than 30 subjects per treatment group and ≤ 3 groups, only the 10 most frequent events in each treatment group are to be listed.
-: Implies that the adverse event was not reported in the particular group or that the adverse event was reported in the particular group but did not fall within the pre-defined counting rule of 10 most frequent events for that group.

* Grade 3 AE: AE that prevented normal activity
** Related AE: AE assessed by the investigator as causally related to the study vaccination

Safety results: Number (%) of subjects with unsolicited adverse events (Total Vaccinated Cohort)

Most frequent adverse events – On-Therapy (occurring within Day 0-20 following vaccination)	**65y+**		**18-40y**
	Flu-1 Group N = 475	**Flu-2 Group N = 488**	**Flu-2 Group N = 289**
Subjects with any AE(s), n (%)	82 (17.3)	68 (13.9)	62 (21.5)
Subjects with grade 3* AE(s), n (%)	7 (1.5)	5 (1.0)	5 (1.7)
Subjects with related** AE(s), n (%)	19 (4.0)	6 (1.2)	11 (3.8)
Upper respiratory tract infection	11 (2.3)	7 (1.4)	6 (2.1)
Nasopharyngitis	10 (2.1)	5 (1.0)	7 (2.4)
Headache	4 (0.8)	-	10 (3.5)
Pharyngolaryngeal pain	3 (0.6)	4 (0.8)	7 (2.4)
Rhinitis	3 (0.6)	5 (1.0)	5 (1.7)
Back pain	3 (0.6)	6 (1.2)	3 (1.0)
Injection site pruritus	7 (1.5)	3 (0.6)	-
Diarrhoea	5 (1.1)	-	2 (0.7)
Cough	4 (0.8)	-	2 (0.7)
Dyspepsia	2 (0.4)	3 (0.6)	-
Rhinorrhoea	-	3 (0.6)	2 (0.7)
Bronchitis	2 (0.4)	-	2 (0.7)
Influenza like illness	-	4 (0.8)	-
Urinary tract infection	-	4 (0.8)	-
Gastroenteritis	-	-	3 (1.0)
Abdominal pain upper	2 (0.4)	-	-
Dizziness	2 (0.4)	-	-
Ear pain	2 (0.4)	-	-
Hyperhidrosis	2 (0.4)	-	-
Injection site pain	2 (0.4)	-	-
Injection site warmth	2 (0.4)	-	-
Migraine	2 (0.4)	-	-
Neck pain	-	-	2 (0.7)
Pain in extremity	2 (0.4)	-	-
Pharyngitis	-	-	2 (0.7)
Pollakiuria	2 (0.4)	-	-
Rash	2 (0.4)	-	-
Sinusitis	2 (0.4)	-	-
Viral infection	-	-	2 (0.7)

Counting rule applied: As there were more than 30 subjects per treatment group and ≤ 3 groups, only the 10 most frequent events in each treatment group are to be listed.
-: Implies that the adverse event was not reported in the particular group or that the adverse event was reported in the

particular group but did not fall within the pre-defined counting rule of 10 most frequent events for that group.
*Grade 3 AE: AE that prevented normal activity
**Related AE: AE considered by the investigator to be causally related to the study vaccination

Safety results: Number (percentage) of subjects with serious adverse events during the vaccination phase of the study (Total Vaccinated Cohort)

All SAEs	**65y+**		**18-40y**
	Flu-1 Group N = 475	**Flu-2 Group N = 488**	**Flu-2 Group N = 289**
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	2 (0.4) [1]	3 (0.6) [0]	1 (0.3) [0]
Ankle fracture	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [0]
Chest pain	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Hip fracture	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Injection site pain	1 (0.2) [1]	0 (0.0) [0]	0 (0.0) [0]
Intervertebral disc degeneration	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Ulna fracture	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	**Flu-1 Group N = 475**	**Flu-2 Group N = 488**	**Flu-2 Group N = 289**
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

Safety results: Number (percentage) of subjects with serious adverse events between Day 21 and Day 179 of the study (Total Vaccinated Cohort)

All SAEs	**65y+**		**18-40y**
	Flu-1 Group N = 475	**Flu-2 Group N = 488**	**Flu-2 Group N = 289**
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	21 (4.4) [0]	24 (4.9) [0]	3 (1.0) [0]
Prostate cancer	1 (0.2) [0]	2 (0.4) [0]	0 (0.0) [0]
Atrial fibrillation	0 (0.0) [0]	2 (0.4) [0]	0 (0.0) [0]
Breast cancer	1 (0.2) [0]	1 (0.2) [0]	0 (0.0) [0]
Chronic obstructive pulmonary disease	2 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Coronary artery disease	1 (0.2) [0]	1 (0.2) [0]	0 (0.0) [0]
Inguinal hernia	0 (0.0) [0]	2 (0.4) [0]	0 (0.0) [0]
Meniscus lesion	0 (0.0) [0]	1 (0.2) [0]	1 (0.3) [0]
Pneumonia	0 (0.0) [0]	2 (0.4) [0]	0 (0.0) [0]
Radius fracture	2 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]
Abdominal hernia	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Abdominal pain	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [0]
Abortion spontaneous	0 (0.0) [0]	0 (0.0) [0]	1 (0.3) [0]
Alcohol withdrawal syndrome	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Angina unstable	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Arthritis	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Bladder cancer	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Bronchitis	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Cardiac failure	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Carotid artery stenosis	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Cellulitis	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Cholecystitis infective	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Contusion	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Coronary artery stenosis	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Cystitis	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Deep vein thrombosis	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Diverticulitis	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Diverticulum	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Dyspnoea	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Enterovesical fistula	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]

Erysipelas	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Haemothorax	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Hydronephrosis	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Hypothyroidism	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Intervertebral disc protrusion	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Joint dislocation	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Large intestine perforation	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Lung carcinoma cell type unspecified stage III	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Mitral valve incompetence	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Multiple fractures	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Multiple injuries	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Non-cardiac chest pain	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Oesophageal ulcer	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Osteomyelitis	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Pelvi-ureteric obstruction	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Pleural effusion	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Pneumothorax	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Precursor b-lymphoblastic lymphoma	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Rectal cancer	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Sick sinus syndrome	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Spinal fusion surgery	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Staphylococcal infection	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Thoracic vertebral fracture	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Ventricular tachycardia	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Vertigo	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Fatal SAES	**Flu-1 Group N = 475**	**Flu-2 Group N = 488**	**Flu-2 Group N = 289**
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	2 (0.4) [0]	0 (0.0) [0]
Mitral valve incompetence	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Precursor b-lymphoblastic lymphoma	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]

Conclusion:
Across groups during the 7-day post-vaccination period, pain was the most frequently reported solicited local symptom; myalgia in 65y+ age sub-group and fatigue in 18-40y age sub-group were the most frequently reported solicited general symptoms.
During the 21-day follow-up period after vaccination, 150 subjects in 65y+ age sub-group [82 (17.3%) in the Flu-1 Group and 68 (13.9%) in the Flu-2 Group] and 62 (21.5%) subjects in the 18-40y age sub-group reported at least one unsolicited AE. SAEs were reported by 5 subjects in the 65y+ age sub-group [2 (0.4%) in the Flu-1 Group and 3 (0.6%) in the Flu-2 Group] and by 1 (0.3%) subject in the 18-40y age sub-group; 1 SAE in an elderly subject from the Flu-1 Group (injection site pain) was assessed by the investigator as related to the study vaccination.
During the long-term follow-up period (Day 21 – 179), SAEs were reported in 45 subjects in 65y+ age sub-group [21 (4.4%) in the Flu-1 Group and 24 (4.9%) in the Flu-2 Group] and 3 (1.0%) subjects in the 18-40y age sub-group; 2 fatal SAEs (mitral valve incompetence and precursor b-lymphoblastic lymphoma) were reported for 2 elderly subjects of the Flu-2 Group. All the fatal and non-fatal SAEs reported during the long-term follow-up period were assessed by the investigators as not related to the study vaccination.

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