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.: 107022 (Flu-LD-001)-107191 (Flu-LD-005)

Title: A phase IIb, controlled, randomised, multicentre, single blind study to demonstrate the non-inferiority of the low dose influenza vaccine with or without adjuvant AS03 compared with Fluarix™ (GlaxoSmithKline Biologicals) administered intramuscularly in elderly ≥ 60 years.
Fluarix™ (Flu): GlaxoSmithKline Biologicals' inactivated influenza split vaccine.

Rationale: The purpose of this study was to evaluate the immunogenicity and safety of low dose of influenza vaccine with or without adjuvant AS03 compared with Flu vaccine administered intramuscularly in elderly subjects aged 60 years and above.

Phase: IIb

Study Period:
Primary study (107022): 11 May 2006 to 18 July 2006 (Data Lock Point – Day 30)
Extension study Day 180 (107191): 06 October 2006 to 19 December 2006

Study Design: Multi-centre, randomised (1:1:1), single blind, controlled study in 3 parallel groups.

Centres:
Primary study (107022): 17 study centres - 11 in Finland and 6 in Greece.
Extension study Day 180 (107191): 15 study centres - 9 in Finland and 6 in Greece.

Indication: Immunization against influenza in male and female subjects aged 60 years and older.

Treatment: The study groups were as follows:

- FluLD-A group: received 1 dose of influenza vaccine adjuvanted with AS03.
- FluLD group: received 1 dose of influenza vaccine non-adjuvanted with AS03.
- Flu group: received 1 dose of Flu vaccine.

All vaccines were administered as a single dose intramuscularly in the deltoid region of the non-dominant arm.

Objectives:

- To demonstrate the immunological non-inferiority [geometric mean titre (GMT)] of the low dose adjuvanted (AS03) influenza vaccine versus Flu vaccine given intramuscularly in elderly (aged ≥ 60 years), 21 days following vaccination.
- To demonstrate the immunological non-inferiority (GMT) of the low dose non-adjuvanted influenza vaccine versus Flu vaccine given intramuscularly in elderly (aged ≥60 years), 21 days following vaccination.

Primary Outcome/Efficacy Variable:
At Days 0 and 21: serum haemagglutination-inhibition (HI) antibody titre, against each of the three vaccine influenza virus strains, in each group.

Secondary Outcome/Efficacy Variable(s):

- At Day 180: serum HI antibody titre, against each of the three vaccine influenza virus strains, in each group.
- Occurrence, intensity 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 and relationship to vaccination of unsolicited adverse events (AEs) during a 30-day follow-up period (i.e. day of vaccination and 29 subsequent days) after vaccination in each group.
- Occurrence and relationship to vaccination of serious adverse events (SAEs) during the entire study period in each group

Statistical Methods:
Analyses were performed on the Total Vaccinated cohort and on the According-To-Protocol (ATP) cohorts for immunogenicity at Day 21 and at Day 180:

- The Total Vaccinated cohort included all vaccinated subjects.
- The ATP cohort for immunogenicity at Day 21 included all evaluable subjects (i.e., those meeting all eligibility criteria, complying with the procedures and intervals defined in the protocol, with no elimination criteria during the study) with available immunogenicity data at Day 21. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination at this time point.
- The ATP cohort for immunogenicity at Day 180 included all evaluable subjects (i.e., those meeting all eligibility criteria, complying with the procedures and intervals defined in the protocol, with no elimination criteria during the study) with available immunogenicity data at Day 180. This included subjects for whom assay results were available

for antibodies against at least one study vaccine antigen component after vaccination at this time point.

Analysis of immunogenicity
The analysis was based on the ATP cohorts for immunogenicity at Day 21 and at Day 180.
Inferential analysis
For each vaccine strain in terms of anti-H1N1(A/New Caledonia), anti-H3N2 (A/New York) and anti-B (B/Malaysia) antibody, the 95% confidence interval (CI) of the GMT ratio (Flu/FluLD-A and Flu/FluLD), 21 days after vaccination, was computed using an analysis of covariance (ANCOVA) model on the logarithm$_{10}$ transformation of the antibody titres. The ANCOVA model included the vaccine group as fixed effect and the pre-vaccination antibody titre as a regressor. The objectives were tested sequentially. This means that the low dose non-adjuvanted influenza vaccine was only compared to the Flu vaccine if the low dose adjuvanted influenza vaccine was shown to be non-inferior to Flu vaccine. The objectives were met if the upper limit of the 95% CI of the GMT ratio was below a pre-specified value of 1.5 in terms of anti-H1N1, anti-H3N2 and anti-B antibody titres.
Descriptive analysis
For each group and each vaccine strain, the following parametres were tabulated: GMTs with 95% CI at Days 0 and 21, seropositivity rate[1] and seroprotection rate (SPR) [2] with exact 95% CI at Days 0 and 21, seroconversion factor (SCF) [3] and seroconversion rate (SCR)[4] with exact 95% CI at Day 21 . The same parameters were tabulated at Day 180. Antibody titres below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculation.
[1]Seropositivity rate was defined as the percentage of subjects with serum HI antibody titres ≥ 1:10.
[2]SPR was defined as the percentage of subjects with serum HI antibody titres ≥ 1:40.
[3]SCF was defined as the fold increase in serum HI GMT on Post-vaccination Day compared to Day 0.
[4]SCR was defined as the percentage of subjects with a pre-vaccination serum HI antibody titres < 1:10 and post-vaccination serum anti-HI titres ≥ 1:40 or pre-vaccination serum anti-HI titres ≥ 1:10 and a fold increase (post/pre) ≥ 4.

Analysis of safety
The analysis was based on the Total Vaccinated cohort.
For each group, the percentage of subjects reporting each individual solicited local and general symptom during the 7-day follow-up period (Days 0-6) was tabulated with exact 95% CI. The same tabulation was performed for grade 3 symptoms and for solicited general symptoms with relationship to vaccination. The percentage of subjects with at least one report of unsolicited AE classified by the Medical Dictionary for Regulatory Activities (MedDRA) and reported up to 30 days (Days 0-29) after vaccination was tabulated. The same tabulation was done for grade 3 and related unsolicited AEs. SAEs during the 30-day post-vaccination period and SAEs from Day 30 up to Day 180 were tabulated per group, according to MedDRA preferred terms.

Study Population: Male or female subject aged 60 years or older at the time of the vaccination, free of an acute aggravation of the health status as established by clinical examination before entering into the study. Subjects with history of confirmed influenza infection within the last 12 months or previously vaccinated against influenza vaccine (2005-2006 influenza vaccine) within 9 months prior to enrollment were excluded. Written informed consent was obtained from the subject.

Number of subjects	**FluLD-A Group**	**FluLD Group**	**Flu Group**
Planned, N	400	400	400
Randomised, N (Total Vaccinated cohort)	407	406	407
Completed (Day 30), n (%)	405 (99.5)	406 (100)	404 (99.3)
Total Number Subjects Withdrawn, n (%)	2 (0.5)	0 (0.0)	3 (0.7)
Withdrawn due to Adverse Events, n (%)	0 (0.0)	0 (0.0)	1 (0.2)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	2 (0.5)	0 (0.0)	2 (0.5)
Demographics	**FluLD-A Group**	**FluLD Group**	**Flu Group**
N (Total Vaccinated cohort)	407	406	407
Females: Males	209:198	205:201	208:199
Mean Age, years (SD)	64.0 (5.12)	64.1 (4.95)	64.2 (5.38)
White/Caucasian, n (%)	407 (100)	405 (99.8)	407 (100)

Primary Efficacy Results:
Non-inferiority of FluLD-A group versus Flu group in terms of GMT ratios at Day 21 for the 3 strains (ATP cohort for immunogenicity at Day 21)

Vaccine strain	**Flu Group**	**FluLD-A Group**	**Adjusted GMT ratio**

					(Flu Group/FluLD-A Group)		
	N	Adjusted GMT	N	Adjusted GMT	Value	95% CI	
						LL	UL*
A/New Caledonia	389	200.2	395	169.8	1.18	0.99	1.40
A/New York	389	102.2	395	183.5	0.56	0.47	0.65
B/Malaysia	389	299.8	394	332.5	0.90	0.77	1.05

Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = number of subjects with both pre-and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio; LL = Lower limit, UL = Upper limit
*Non-inferiority criterion: UL of the 95% CI of the GMT ratio (Flu over FluLD-A) < 1.5

Primary Efficacy Results:
Non-inferiority of FluLD group vaccine versus Flu group in terms of GMT ratios at Day 21 for the 3 strains (ATP cohort for immunogenicity at Day 21)

Vaccine strain	Flu Group		FluLD Group		Adjusted GMT ratio (Flu Group/FluLD Group)		
	N	Adjusted GMT	N	Adjusted GMT	Value	95% CI	
						LL	UL*
A/New Caledonia	389	201.5	393	98.1	2.05	1.72	2.46
A/New York	389	105.2	393	69.8	1.51	1.27	1.79
B/Malaysia	389	293.7	390	174.3	1.68	1.43	1.99

Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = number of subjects with both pre-and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio; LL = Lower limit, UL = Upper limit
*Non-inferiority criterion: UL of the 95% CI of the GMT ratio (Flu over FluLD) < 1.5

Primary Efficacy Results:
Seropositivity rates and GMTs for HI antibody titre at Day 0 and Day 21 (ATP cohort for immunogenicity at Day 21)

Vaccine strain	Group	Timing	N	≥ 1:10				GMT		
				n	%	95% CI		value	95% CI	
						LL	UL		LL	UL
A/New Caledonia	FluLD-A	PRE	395	278	70.4	65.6	74.8	13.4	12.3	14.8
		PI(D21)	395	394	99.7	98.6	100	168.0	148.5	190.1
	FluLD	PRE	393	282	71.8	67.0	76.2	13.9	12.6	15.3
		PI(D21)	393	386	98.2	96.4	99.3	97.7	85.7	111.3
	Flu	PRE	389	282	72.5	67.8	76.9	14.2	13.0	15.6
		PI(D21)	389	387	99.5	98.2	99.9	202.4	177.4	230.9
A/New York	FluLD-A	PRE	395	229	58.0	52.9	62.9	10.8	9.9	11.8
		PI(D21)	395	391	99.0	97.4	99.7	179.8	159.3	202.9
	FluLD	PRE	393	235	59.8	54.8	64.7	11.9	10.7	13.1
		PI(D21)	393	373	94.9	92.2	96.9	70.4	61.3	80.7
	Flu	PRE	389	231	59.4	54.3	64.3	11.5	10.5	12.7
		PI(D21)	389	383	98.5	96.7	99.4	104.3	91.5	118.9
B/Malaysia	FluLD-A	PRE	395	297	75.2	70.6	79.4	17.8	16.0	19.7
		PI(D21)	394	394	100	99.1	100	341.2	305.7	380.9
	FluLD	PRE	393	273	69.5	64.7	74.0	16.0	14.4	17.8
		PI(D21)	390	386	99.0	97.4	99.7	175.4	154.1	199.5
	Flu	PRE	389	261	67.1	62.2	71.7	15.6	14.0	17.4
		PI(D21)	389	387	99.5	98.2	99.9	292.0	257.1	331.5

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

Primary Efficacy Results:
Seroconversion factor for HI antibody titre at Day 21 (ATP cohort for immunogenicity at Day 21)

Vaccine strain	Group	N	SCF	95% CI	
				LL	UL

A/New Caledonia	FluLD-A	395	12.5	11.0	14.2
	FluLD	393	7.0	6.1	8.1
	Flu	389	14.2	12.4	16.4
A/New York	FluLD-A	395	16.7	14.9	18.7
	FluLD	393	5.9	5.2	6.7
	Flu	389	9.0	8.0	10.2
B/Malaysia	FluLD-A	394	19.3	17.1	21.7
	FluLD	390	11.0	9.6	12.5
	Flu	389	18.7	16.4	21.4

SCF= fold increase in HI GMTs on Day 21 compared to Day 0
N = number of subjects with available results
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Primary Efficacy Results:
Seroconversion rate for HI antibody titre at Day 21 (ATP cohort for immunogenicity at Day 21)

Vaccine strain	**Group**	**N**	**SCR**			
			n	**%**	**95% CI**	
					LL	**UL**
A/New Caledonia	FluLD-A	395	315	79.7	75.4	83.6
	FluLD	393	244	62.1	57.1	66.9
	Flu	389	314	80.7	76.4	84.5
A/New York	FluLD-A	395	343	86.8	83.1	90.0
	FluLD	393	229	58.3	53.2	63.2
	Flu	389	275	70.7	65.9	75.2
B/Malaysia	FluLD-A	394	355	90.1	86.7	92.9
	FluLD	390	299	76.7	72.1	80.8
	Flu	389	341	87.7	84.0	90.8

SCR defined as the percentage of subjects with a pre-vaccination serum HI antibody titres < 1:10 and post-vaccination serum anti-HI titres ≥ 1:40 or pre-vaccination serum anti-HI titres ≥ 1:10 and a fold increase (post/pre) ≥ 4.
N = number of subjects with available results
n (%) = number (percentage) of subjects who seroconverted post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Primary Efficacy Results:
Seroprotection rates for HI antibody titre at each time point (ATP cohort for immunogenicity at Day 21)

Vaccine strain	**Group**	**Timing**	**N**	**SPR**			
				n	**%**	**95% CI**	
						LL	**UL**
A/New Caledonia	FluLD-A	PRE	395	54	13.7	10.44	17.46
		PI(D21)	395	362	91.6	88.47	94.18
	FluLD	PRE	393	60	15.3	11.86	19.21
		PI(D21)	393	311	79.1	74.78	83.05
	Flu	PRE	389	65	16.7	13.14	20.80
		PI(D21)	389	362	93.1	90.06	95.38
A/New York	FluLD-A	PRE	395	43	10.9	7.99	14.38
		PI(D21)	395	361	91.4	88.18	93.97
	FluLD	PRE	393	51	13.0	9.82	16.71
		PI(D21)	393	279	71.0	66.23	75.43
	Flu	PRE	389	56	14.4	11.06	18.28
		PI(D21)	389	318	81.7	77.54	85.46
B/Malaysia	FluLD-A	PRE	395	103	26.1	21.81	30.70
		PI(D21)	394	388	98.5	96.72	99.44
	FluLD	PRE	393	98	24.9	20.73	29.52
		PI(D21)	390	353	90.5	87.16	93.23
	Flu	PRE	389	92	23.7	19.51	28.19
		PI(D21)	389	376	96.7	94.35	98.21

N = number of subjects with available results
n (%) = number (percentage) of seroprotected subjects (HI antibody titre ≥ 1:40)

95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination at Day 0
PI(D21) = post-vaccination at Day 21

Secondary Outcome Variable(s):
Seropositivity rates and GMTs for HI antibody titre at each time point (ATP cohort for immunogenicity at Day 180)

Vaccine strain	Group	Timing	N	≥ 1:10				GMT		
				n	%	95% CI		value	95% CI	
						LL	UL		LL	UL
A/New Caledonia	FluLD-A	PRE	389	273	70.2	65.4	74.7	13.3	12.1	14.6
		PI(D21)	389	388	99.7	98.6	100	168.2	148.4	190.6
		PI(D180)	389	387	99.5	98.2	99.9	64.3	57.6	71.8
	FluLD	PRE	386	276	71.5	66.7	76.0	14.0	12.7	15.4
		PI(D21)	386	380	98.4	96.6	99.4	98.2	86.1	112.1
		PI(D180)	383	376	98.2	96.3	99.3	54.3	48.3	61.0
	Flu	PRE	382	278	72.8	68.0	77.2	14.2	12.9	15.5
		PI(D21)	382	380	99.5	98.1	99.9	204.8	179.2	234.0
		PI(D180)	380	373	98.2	96.2	99.3	84.4	74.8	95.3
A/New York	FluLD-A	PRE	389	226	58.1	53.0	63.1	10.8	9.9	11.8
		PI(D21)	389	385	99.0	97.4	99.7	181.1	160.3	204.6
		PI(D180)	389	380	97.7	95.7	98.9	56.8	50.9	63.5
	FluLD	PRE	386	231	59.8	54.8	64.8	12.0	10.8	13.2
		PI(D21)	386	367	95.1	92.4	97.0	71.1	61.9	81.7
		PI(D180)	383	350	91.4	88.1	94.0	35.8	31.7	40.3
	Flu	PRE	382	228	59.7	54.6	64.6	11.5	10.5	12.7
		PI(D21)	382	376	98.4	96.6	99.4	104.8	91.8	119.7
		PI(D180)	380	360	94.7	92.0	96.8	42.4	37.7	47.6
B/Malaysia	FluLD-A	PRE	389	292	75.1	70.5	79.3	17.6	15.8	19.5
		PI(D21)	388	388	100	99.1	100	343.4	307.2	383.8
		PI(D180)	389	382	98.2	96.3	99.3	88.6	79.0	99.3
	FluLD	PRE	386	268	69.4	64.6	74.0	15.9	14.3	17.8
		PI(D21)	383	379	99.0	97.3	99.7	174.2	153.0	198.5
		PI(D180)	383	370	96.6	94.3	98.2	65.2	58.0	73.3
	Flu	PRE	382	257	67.3	62.3	72.0	15.5	13.9	17.3
		PI(D21)	382	380	99.5	98.1	99.9	292.8	257.8	332.6
		PI(D180)	380	375	98.7	97.0	99.6	90.9	80.7	102.5

N = number of subjects with available results
n (%) = number (percentage) of seropositive subjects (HI antibody titre ≥ 1:10)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination at Day 0
PI(D21) = post-vaccination at Day 21
PI(D180) = post-vaccination at Day 180

Secondary Outcome Variable(s):
Seroconversion factor for HI antibody titre at Day 21 and Day 180 (ATP cohort for immunogenicity at Day 180)

Vaccine strain	Group	Timing	N	SCF		
				Value	95% CI	
					LL	UL
A/New Caledonia	FluLD-A	PI(D21)	389	12.6	11.1	14.4
		PI(D180)	389	4.8	4.3	5.4
	FluLD	PI(D21)	386	7.0	6.1	8.1
		PI(D180)	383	3.9	3.5	4.4
	Flu	PI(D21)	382	14.5	12.6	16.6
		PI(D180)	380	6.0	5.3	6.7
A/New York	FluLD-A	PI(D21)	389	16.7	14.9	18.8
		PI(D180)	389	5.3	4.8	5.8
	FluLD	PI(D21)	386	6.0	5.2	6.7

		PI(D180)	383	3.0	2.7	3.4
	Flu	PI(D21)	382	9.1	8.0	10.3
		PI(D180)	380	3.7	3.3	4.1
B/Malaysia	FluLD-A	PI(D21)	388	19.6	17.4	22.1
		PI(D180)	389	5.0	4.5	5.7
	FluLD	PI(D21)	383	11.0	9.6	12.5
		PI(D180)	383	4.1	3.7	4.6
	Flu	PI(D21)	382	18.9	16.5	21.6
		PI(D180)	380	5.9	5.2	6.7

SCF= fold increase in HI GMTs on Post-vaccination Day compared to Day 0
N = number of subjects with pre- and post-vaccination results available
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D21) = post-vaccination at Day 21
PI(D180) = post-vaccination at Day 180

Secondary Outcome Variable(s):
Seroconversion rate for HI antibody titre at Day 21 and Day 180 (ATP cohort for immunogenicity at Day 180)

Vaccine strain	**Group**	**Timing**	**N**	**SCR**			
				n	**%**	**95% CI**	
						LL	**UL**
A/New Caledonia	FluLD-A	PI(D21)	389	310	79.7	75.3	83.6
		PI(D180)	389	192	49.4	44.3	54.4
	FluLD	PI(D21)	386	238	61.7	56.6	66.5
		PI(D180)	383	165	43.1	38.1	48.2
	Flu	PI(D21)	382	310	81.2	76.9	85.0
		PI(D180)	380	239	62.9	57.8	67.8
A/New York	FluLD-A	PI(D21)	389	337	86.6	82.8	89.9
		PI(D180)	389	222	57.1	52.0	62.0
	FluLD	PI(D21)	386	224	58.0	52.9	63.0
		PI(D180)	383	140	36.6	31.7	41.6
	Flu	PI(D21)	382	271	70.9	66.1	75.4
		PI(D180)	380	151	39.7	34.8	44.9
B/Malaysia	FluLD-A	PI(D21)	388	351	90.5	87.1	93.2
		PI(D180)	389	225	57.8	52.8	62.8
	FluLD	PI(D21)	383	293	76.5	71.9	80.7
		PI(D180)	383	188	49.1	44.0	54.2
	Flu	PI(D21)	382	337	88.2	84.6	91.3
		PI(D180)	380	233	61.3	56.2	66.2

SCR defined as the percentage of subjects with a pre-vaccination serum HI antibody titres < 1:10 and post-vaccination serum anti-HI titres ≥ 1:40 or pre-vaccination serum anti-HI titres ≥ 1:10 and a fold increase (post/pre) ≥ 4.
N = number of subjects with pre- and post-vaccination results available
n (%) = number (percentage) of subjects who seroconverted
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PI(D21) = post-vaccination at Day 21
PI(D180) = post-vaccination at Day 180

Secondary Outcome Variable(s):
Seroprotection rates for HI antibody titre at each time point (ATP cohort for immunogenicity at Day 180)

Vaccine strain	**Group**	**Timing**	**N**	**SPR**			
				n	**%**	**95% CI**	
						LL	**UL**
A/New Caledonia	FluLD-A	PRE	389	51	13.1	9.9	16.9
		PI(D21)	389	356	91.5	88.3	94.1
		PI(D180)	389	280	72.0	67.2	76.4
	FluLD	PRE	386	60	15.5	12.1	19.6
		PI(D21)	386	305	79.0	74.6	83.0
		PI(D180)	383	250	65.3	60.3	70.0
	Flu	PRE	382	63	16.5	12.9	20.6

		PI(D21)	382	355	92.9	89.9	95.3
		PI(D180)	380	312	82.1	77.9	85.8
A/New York	FluLD-A	PRE	389	43	11.1	8.1	14.6
		PI(D21)	389	355	91.3	88.0	93.9
		PI(D180)	389	265	68.1	63.2	72.7
	FluLD	PRE	386	51	13.2	10.0	17.0
		PI(D21)	386	274	71.0	66.2	75.5
		PI(D180)	383	202	52.7	47.6	57.8
	Flu	PRE	382	54	14.1	10.8	18.0
		PI(D21)	382	312	81.7	77.4	85.4
		PI(D180)	380	220	57.9	52.8	62.9
B/Malaysia	FluLD-A	PRE	389	101	26.0	21.7	30.6
		PI(D21)	388	382	98.5	96.7	99.4
		PI(D180)	389	316	81.2	77.0	85.0
	FluLD	PRE	386	94	24.4	20.2	29.0
		PI(D21)	383	347	90.6	87.2	93.3
		PI(D180)	383	283	73.9	69.2	78.2
	Flu	PRE	382	90	23.6	19.4	28.1
		PI(D21)	382	370	96.9	94.6	98.4
		PI(D180)	380	319	83.9	79.9	87.5

N = number of subjects with available results
n (%) = number (percentage) of seroprotected subjects (HI antibody titre ≥ 1:40)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = pre-vaccination at Day 0
PI(D21) = post-vaccination at Day 21
PI(D180) = post-vaccination at Day 180

Secondary Outcome Variable(s):
Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort)

Symptom	**Intensity**	**FluLD-A Group (N = 405)**				**FluLD Group (N = 404)**				**Flu Group (N = 406)**			
		n	**%**	**95 % CI**		**n**	**%**	**95 % CI**		**n**	**%**	**95 % CI**	
				LL	**UL**			**LL**	**UL**			**LL**	**UL**
Ecchymosis	Any	28	6.9	4.6	9.8	20	5.0	3.0	7.5	19	4.7	2.8	7.2
	> 50 mm	1	0.2	0.0	1.4	0	0.0	0.0	0.9	1	0.2	0.0	1.4
Pain	Any	246	60.7	55.8	65.5	32	7.9	5.5	11.0	86	21.2	17.3	25.5
	Grade 3	12	3.0	1.5	5.1	0	0.0	0.0	0.9	1	0.2	0.0	1.4
Redness	Any	95	23.5	19.4	27.9	50	12.4	9.3	16.0	65	16.0	12.6	19.9
	> 50 mm	22	5.4	3.4	8.1	1	0.2	0.0	1.4	6	1.5	0.5	3.2
Swelling	Any	84	20.7	16.9	25.0	8	2.0	0.9	3.9	50	12.3	9.3	15.9
	> 50 mm	19	4.7	2.8	7.2	0	0.0	0.0	0.9	4	1.0	0.3	2.5

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 = incidence of a particular symptom regardless of intensity grade
Grade 3 Pain = pain that prevented normal activity

Secondary Outcome Variable(s):
Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort)

Symptom	**Intensity/ Relationship**	**FluLD-A Group (N = 405)**				**FluLD Group (N = 404)**				**Flu Group (N = 406)**			
		n	**%**	**95 % CI**		**n**	**%**	**95 % CI**		**n**	**%**	**95 % CI**	
				LL	**UL**			**LL**	**UL**			**LL**	**UL**
Arthralgia	Any	80	19.8	16.0	24.0	17	4.2	2.5	6.7	21	5.2	3.2	7.8
	Grade 3	6	1.5	0.5	3.2	0	0.0	0.0	0.9	1	0.2	0.0	1.4
	Related	73	18.0	14.4	22.1	14	3.5	1.9	5.7	18	4.4	2.6	6.9
Fatigue	Any	149	36.8	32.1	41.7	42	10.4	7.6	13.8	47	11.6	8.6	15.1
	Grade 3	6	1.5	0.5	3.2	1	0.2	0.0	1.4	0	0.0	0.0	0.9

	Related	148	36.5	31.8	41.4	36	8.9	6.3	12.1	42	10.3	7.6	13.7
Fever (orally)	≥ 37.5°C	21	5.2	3.2	7.8	4	1.0	0.3	2.5	2	0.5	0.1	1.8
	> 39.0°C	0	0.0	0.0	0.9	0	0.0	0.0	0.9	0	0.0	0.0	0.9
	Related	21	5.2	3.2	7.8	2	0.5	0.1	1.8	1	0.2	0.0	1.4
Headache	Any	104	25.7	21.5	30.2	51	12.6	9.5	16.3	53	13.1	9.9	16.7
	Grade 3	5	1.2	0.4	2.9	0	0.0	0.0	0.9	1	0.2	0.0	1.4
	Related	100	24.7	20.6	29.2	45	11.1	8.2	14.6	46	11.3	8.4	14.8
Muscle aches	Any	129	31.9	27.3	36.6	31	7.7	5.3	10.7	38	9.4	6.7	12.6
	Grade 3	6	1.5	0.5	3.2	0	0.0	0.0	0.9	0	0.0	0.0	0.9
	Related	125	30.9	26.4	35.6	28	6.9	4.7	9.9	36	8.9	6.3	12.1
Shivering	Any	95	23.5	19.4	27.9	19	4.7	2.9	7.2	26	6.4	4.2	9.2
	Grade 3	10	2.5	1.2	4.5	1	0.2	0.0	1.4	1	0.2	0.0	1.4
	Related	94	23.2	19.2	27.6	17	4.2	2.5	6.7	22	5.4	3.4	8.1

N = number of subjects with the documented dose
n (%) = number (percentage) of subjects reporting the symptom at least once
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Any = incidence of a particular symptom regardless of intensity grade or relationship with the study vaccination
Grade 3 symptom = symptom that prevented normal activity
Related = symptom considered by the investigator to have a causal relationship to study vaccination

Safety Results: Number (%) of subjects with unsolicited AEs during the 30-day post-vaccination period (Total Vaccinated cohort)

Most frequent adverse events–On-Therapy (occurring within Days 0-29 following vaccination)	**FluLD-A Group N = 407**	**FluLD Group N = 406**	**Flu Group N = 407**
Subjects with any AE(s), n (%)	114 (28.0)	82 (20.2)	95 (23.3)
Subjects with any Grade 3 AE(s), n (%)	13 (3.2)	11 (2.7)	16 (3.9)
Subjects with any related AE(s), n (%)	43 (10.6)	19 (4.7)	19 (4.7)
Back pain	13 (3.2)	9 (2.2)	9 (2.2)
Headache	6 (1.5)	10 (2.5)	13 (3.2)
Upper respiratory tract infection	9 (2.2)	3 (0.7)	7 (1.7)
Rhinitis	8 (2.0)	5 (1.2)	4 (1.0)
Arthralgia	8 (2.0)	3 (0.7)	-
Pharyngolaryngeal pain	8 (2.0)	4 (1.0)	-
Pain in extremity	-	5 (1.2)	4 (1.0)
Injection site pruritus	5 (1.2)	3 (0.7)	-
Cough	-	4 (1.0)	4 (1.0)
Shoulder pain	4 (1.0)	3 (0.7)	-
Respiratory tract infection	4 (1.0)	-	4 (1.0)
Neck pain	-	-	5 (1.2)
Dyspepsia	-	-	4 (1.0)
Muscle spasms	-	4 (1.0)	-
Myalgia	-	-	5 (1.2)
Diarrhoea	-	3 (0.7)	-
Vomiting	-	-	4 (1.0)
Lymphadenopathy	4 (1.0)	-	-

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 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 (%) of subjects with SAEs within the 30-day post-vaccination period (Total Vaccinated cohort)-)

Serious adverse event, n (%) [n considered by the investigator to be related to study medication]

All SAEs	**FluLD-A Group N = 407**	**FluLD Group N = 406**	**Flu Group N = 407**
Subjects with any SAE(s), n (%) [n assessed by investigators as related]	2 (0.5) [1]	1 (0.2) [1]	2 (0.5) [0]

Abdominal pain	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]
Gastric ulcer	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Gastrointestinal haemorrhage	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Gastrooesophageal reflux disease	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Grand mal convulsion	0 (0.0) [0]	1 (0.2) [1]	0 (0.0) [0]
Injection site erythema	1 (0.2) [1]	0 (0.0) [0]	0 (0.0) [0]
Pancreatic neoplasm	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]
Pulmonary embolism	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]
Pyrexia	1 (0.2) [1]	0 (0.0) [0]	0 (0.0) [0]
Fatal saes	**FluLD-A Group N = 407**	**FluLD Group N = 406**	**Flu Group N = 407**
Subjects with fatal SAE(s), n (%) [n assessed by investigators as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Safety Results: Number (%) of subjects with SAEs from Day 30 to Day 180 (Total Vaccinated cohort)			
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]			
All SAEs	**FluLD-A Group N = 407**	**FluLD Group N = 406**	**Flu Group N = 407**
Subjects with any SAE(s), n (%) [n assessed by investigators as related]	6 (1.5) [1]	12 (3.0) [0]	11 (2.7) [0]
Cerebral infarction	2 (0.5) [0]*	0 (0.0) [0]	1 (0.2) [0]*
Breast cancer	0 (0.0) [0]	1 (0.2) [0]	1 (0.2) [0]
Cholecystitis	1 (0.2) [0]	1 (0.2) [0]	0 (0.0) [0]
Arthralgia	1 (0.2) [1]	0 (0.0) [0]	0 (0.0) [0]
Asthma	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]
Brain stem thrombosis	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Cardiac failure	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]*
Cholelithiasis	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Concussion	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]
Dermatitis allergic	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]
Diverticulitis	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Drowning	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]*
Extrasystoles	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]
Femoral neck fracture	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Gastric ulcer	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]
Irritable bowel syndrome	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]
Lung neoplasm malignant	0 (0.0) [0]	1 (0.2) [0]*	0 (0.0) [0]
Myocardial infarction	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Pancreatitis	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]
Peptic ulcer	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Polymyalgia rheumatica	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Prostate cancer	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Pyelonephritis	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Skull fracture	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Subarachnoid haemorrhage	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Uterine neoplasm	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]
Wrist fracture	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]
Fatal SAEs	**FluLD-A Group N = 407**	**FluLD Group N = 406**	**Flu Group N = 407**
Subjects with fatal SAE(s), n (%) [n assessed by investigators as related]	0 (0.0) [0]	1 (0.2) [0]	2 (0.5) [0]
Cardiac failure	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]*
Drowning	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]*
Lung neoplasm malignant	0 (0.0) [0]	1 (0.2) [0]*	0 (0.0) [0]
*SAEs reported by 5 subjects who did not complete the follow-up period and were not included in the Total Vaccinated			

Cohort

Conclusion:
On Day 21, the GMTs for HI antibodies were at least 97.7, 70.4 & 175.4 for vaccine strains A/New Caledonia, A/New York & B/Malaysia, respectively**.** At the same time point, at least 79.1%, 71.0% and 90.5% of the subjects had HI antibody titers ≥ 1:40 for vaccine strains A/New Caledonia, A/New York and B/Malaysia, respectively. On Day 180, the GMTs for HI antibodies were at least 54.3, 35.8 & 65.2 for vaccine strains A/New Caledonia, A/New York & B/Malaysia, respectively**.** At the same time point, at least 65.3%, 52.7% & 73.9% of the subjects had HI antibody titers ≥ 1:40 for vaccine strains A/New Caledonia, A/New York and B/Malaysia, respectively. Unsolicited AEs were reported for 114 (28.0%), 82 (20.2%) and 95 (23.3%) subjects in the FluLD-A, FluLD and Flu groups. Within the 30-day post-vaccination period, SAEs were reported by 2(0.5%) subjects in the FluLD-A Group, 1 (0.2%) subject in the FluLD Group and 2 (0.5%) subjects in the Flu Group; of these, the SAEs in 1 subject in the FluLD-A Group and the SAE in the FluLD Group, were considered by the investigators to be related to the study vaccination.
Between Day-31 and Day-180 after vaccination, SAEs were reported by 6 (1.5), 12 (3.0%) and 11 (2.7%) subjects in FluLD-A, FluLD and Flu groups, respectively; 1 SAE in the FluLD-A Group was considered by the investigator to be causally related to the study vaccination. Fatal SAEs were reported for 1 (0.2%) and 2 (0.5%) subjects in the FluLD and Flu groups, respectively; the fatal SAEs were considered by the investigators to be not related to the study vaccination. No fatal SAEs were reported in the FluLD-A group.

Date updated: 21-July-2014