

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.: 107564
Title: An observational study to investigate the incidence of influenza and influenza-related complications, in adults between 50-64 years and elderly adults 65 years and over vaccinated with GSK Biologicals' influenza vaccine (Fluarix™) administered intramuscularly. Fluarix™ (Flu): GlaxoSmithKline (GSK) Biologicals' trivalent inactivated split virion influenza vaccine.
Rationale: The aim of this study was to investigate the incidence of influenza, influenza like illness (ILI) and various possible influenza-related complications such as pneumonia, ischemic heart disease (unstable angina or myocardial infarction), congestive heart failure, acute cerebrovascular disease and exacerbation of chronic obstructive pulmonary disease (COPD) as well as mortality. In addition, health resource utilization such as hospitalizations, emergency room visits, and unscheduled ILI-or influenza-related medical office visits was assessed. The incidence of laboratory confirmed Respiratory Syncytial Virus (RSV) infection in subjects ≥ 50 years after vaccination with Flu vaccine was also evaluated.
Phase: Epidemiology
Study Period: 5 October 2006 to 20 June 2007.
Study Design: Multi-centre, open-label, observational study with 1 study group.
Centers: 37 study centers: 21 in Germany (GE), 9 in The United States (US), 6 in Poland (PL) and 1 in The Netherlands (NL).
Indication: Immunization against influenza in male and female subjects aged ≥ 50 years.
Treatment: All subjects received a single dose of Flu vaccine by intramuscular injection into the deltoid region of the non-dominant arm.
Objectives: <i>During the influenza season and during the surveillance period, in subjects ≥ 50 years, after vaccination with Flu vaccine:</i> <ul style="list-style-type: none"> • To evaluate the incidence of ILI. • To evaluate the incidence of laboratory confirmed influenza; laboratory confirmation was by detection of influenza A and /or B by virus culture and/or reverse transcriptase-polymerase chain reaction (RT-PCR) in nasal and throat swab specimens or equivalent specimen. • To evaluate the incidence of hospitalizations, emergency room visits, or unscheduled medical office visits due to ILI. • To evaluate the incidence of hospitalizations, emergency room visits or unscheduled medical office visits due to laboratory confirmed influenza. • To evaluate the frequency of hospitalization or emergency room visit for any cause. • To evaluate the incidence of pneumonia, ischemic heart disease (unstable angina or myocardial infarction), congestive heart failure, acute cerebrovascular disease and COPD exacerbation. • To evaluate the incidence of hospitalizations, emergency room visits, or unscheduled medical office visits due to pneumonia, ischemic heart disease (unstable angina or myocardial infarction), congestive heart failure, acute cerebrovascular disease and COPD exacerbation. • To evaluate the mortality due to laboratory confirmed influenza infection. • To evaluate all-cause mortality in the study cohort. • To evaluate the incidence of laboratory confirmed RSV infection; laboratory confirmation was by detection of RSV by RT-PCR in nasal and throat swab specimens or equivalent specimen. Safety <ul style="list-style-type: none"> • To evaluate the safety of one dose of Flu vaccine in terms of occurrence of serious adverse events (SAE) following the intramuscular administration in subjects ≥ 50 years. Immunogenicity <ul style="list-style-type: none"> • To evaluate the immune response in terms of haemagglutinin inhibition (HI) antibody after vaccination with Flu vaccine in a subset of subjects ≥ 50 years.
Primary Outcome/Efficacy Variable: <i>During the influenza season and during the surveillance period, in subjects ≥ 50 years, after vaccination with Flu vaccine:</i> <ul style="list-style-type: none"> • Incidence of ILI. • Incidence of laboratory-confirmed influenza A and/or B infection (viral culture and/or RT-PCR). • Incidence of hospitalizations, emergency room visits, or unscheduled medical office visits due to ILI. • Incidence of hospitalizations, emergency room visits or unscheduled medical office visits, due to laboratory confirmed

influenza.

- Incidence of hospitalization or emergency room visit for any cause.
- Incidence of pneumonia, ischemic heart disease (unstable angina or myocardial infarction), congestive heart failure, acute cerebrovascular disease and COPD exacerbation.
- Incidence of hospitalizations, emergency room visits, or unscheduled medical office visits due to pneumonia, ischemic heart disease (unstable angina or myocardial infarction), congestive heart failure, acute cerebrovascular disease and chronic obstructive pulmonary disease (COPD) exacerbation.
- Number of deaths due to laboratory confirmed influenza infection.
- Number of deaths.
- Incidence of laboratory-confirmed RSV infection (RT-PCR).

Safety

- Occurrence of SAEs in all subjects during the entire study.

Immunogenicity in a subset of subjects

- For each vaccine strain, seroconversion rate with 95% confidence interval (CI) at Day 21 defined as the proportion of subjects with either a pre-vaccination HI titer < 1:10 and a post-vaccination titer \geq 1:40, or a pre-vaccination titer \geq 1:10 and a minimum four-fold increase in post-vaccination titer.
- For each vaccine strain, seroconversion factor at Day 21 defined as the fold increase in serum HI antibody geometric mean titer (GMT) on Day 21 compared to Day 0.
- For each vaccine strain, seroprotection rate with 95% CI at Day 0 and Day 21 defined as the proportion of vaccinees with a serum HI titer \geq 1:40.
- For each vaccine strain, GMT of serum HI antibodies with 95% CI pre- and post-vaccination.

Secondary Outcome/Efficacy Variable(s):

Not applicable.

Statistical Methods:

The analyses were performed on the Total Vaccinated Cohort and the According-to-Protocol (ATP) cohort for immunogenicity.

- The Total Vaccinated Cohort included all subjects with one vaccine administration documented, for whom data were available.
- The ATP cohort for analysis of immunogenicity included all evaluable subjects (i.e. those meeting all eligibility criteria, complying with the procedures defined in the protocol, with no elimination criteria during the study) for whom data concerning immunogenicity measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination.

Analysis of epidemiology

The analyses were performed on the Total vaccinated cohort.

The following criteria were computed for each country and overall for all subjects having received the Flu vaccine during the influenza season.

- Proportion of subjects with culture and/or RT-PCR confirmed influenza A and/or B infection having received Flu vaccination prior to influenza season and 95% CI.
- Proportion of subjects with pneumonia, ischemic heart disease (unstable angina or myocardial infarction), congestive heart failure, acute cerebrovascular disease, or COPD exacerbation and 95% CI.
- Proportion of death and death due to influenza during surveillance period and 95% CI.
- Proportion of subjects with ILI having received Flu vaccination prior to influenza season and 95% CI.
- Proportion of subjects with RSV having received Flu vaccination prior to influenza season and 95% CI.
- Proportion of subjects with any hospitalization or emergency room visit, hospitalization or emergency room visit due to ILI, unscheduled ILI-related medical office visit, hospitalization, emergency room visit or unscheduled medical office visit with laboratory confirmed influenza infection, and hospitalization, emergency room visit or unscheduled medical office visit due to pneumonia, ischemic HD (unstable angina or MI), congestive heart failure, acute cerebrovascular disease, or COPD exacerbation and 95% CI.

Analysis of immunogenicity (only for a subset of subjects)

The analyses were performed on the ATP cohort for immunogenicity.

For each vaccine strain, the Geometric mean serum HI titer at Day 21, Seroconversion rate (SCR) at Day 21, Seroconversion factor (SCF) at Day 21 and Seroprotection rate (SPR) at Day 0 and Day 21 with their 95% CI were tabulated.

Analysis of safety

- The occurrence of SAEs during the entire study period was tabulated on the Total Vaccinated Cohort, according to Medical Dictionary of Regulatory Activities (MedDRA) preferred terms.

Study Population: Male or female subjects aged ≥ 50 years at the time of the first vaccination and with residence status allowing free mixing with general community were enrolled. If female, the subject had to be of non-childbearing potential; or, if of childbearing potential, she had to be abstinent or have used adequate contraceptive precautions for 30 days prior to vaccination, have a negative pregnancy test and had to agree to continue such precautions for 2 months after vaccination. Subjects with a history of hypersensitivity to a previous dose of influenza vaccine, with a history of allergy or reactions likely to be exacerbated by any component of the vaccine or with any contra-indication to intramuscular administration of Flu vaccine were excluded from the study. Written informed consent was obtained from the subject.

	Germany			Netherlands		
Number of subjects	50-64y	65y+	50y+	50-64y	65y+	50y+
Planned, N	250	500	750	250	500	750
Randomized, N (Total Vaccinated Cohort)	297	697	994	286	449	735
Completed, n (%)	295 (99.3)	688 (98.7)	983 (98.9)	271 (94.8)	434 (96.7)	705 (95.9)
Total Number Subjects Withdrawn, n (%)	2 (0.7)	9 (1.3)	11 (1.1)	15 (5.2)	15 (3.3)	30 (4.1)
Withdrawn due to Adverse Events, n (%)	0	8 (1.1)	8 (0.8)	0	0	0
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	2 (0.7)	1 (0.1)	3 (0.3)	15 (5.2)	15 (3.3)	30 (4.1)
Demographics	50-64y	65y+	50y+	50-64y	65y+	50y+
N (Total Vaccinated Cohort)	297	697	994	286	449	735
Females:Males	164:133	372:325	536:458	146:140	232:217	378:357
Mean Age, years (SD)	57.8 (4.33)	69.9 (4.39)	66.3 (7.06)	57.7 (3.82)	70.7 (4.67)	65.6 (7.68)
White - Caucasian / European heritage, n (%)	297 (100)	688 (98.7)	985 (99.1)	276 (96.5)	440 (98.0)	716 (97.4)
	Poland			United States		
Number of subjects	50-64y	65y+	50y+	50-64y	65y+	50y+
Planned, N	250	500	750	250	500	750
Randomized, N (Total Vaccinated Cohort)	290	497	787	174	364	538
Completed, n (%)	289 (99.7)	496 (99.8)	785 (99.7)	170 (97.7)	356 (97.8)	526 (97.8)
Total Number Subjects Withdrawn, n (%)	1 (0.3)	1 (0.2)	2 (0.3)	4 (2.3)	8 (2.2)	12 (2.2)
Withdrawn due to Adverse Events, n (%)	0	1 (0.2)	1 (0.1)	2 (1.1)	0	2 (0.4)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	1 (0.3)	0	1 (0.1)	2 (1.1)	8 (2.2)	10 (1.9)
Demographics	50-64y	65y+	50y+	50-64y	65y+	50y+
N (Total Vaccinated Cohort)	290	497	787	174	364	538
Females:Males	182:108	292:205	474:313	107:67	198:166	305:233
Mean Age, years (SD)	57.4 (3.95)	70.3 (4.09)	65.5 (7.38)	57.6 (4.47)	70.5 (4.59)	66.3 (7.54)
White - Caucasian / European heritage, n (%)	290 (100)	497 (100)	787 (100)	152 (87.4)	335 (92.0)	487 (90.5)
	Total					
Number of subjects	50-64y		65y+		50y+	
Planned, N	1000		2000		3000	
Randomized, N (Total Vaccinated Cohort)	1047		2007		3054	
Completed, n (%)	1025 (97.9)		1974 (98.4)		2999 (98.2)	
Total Number Subjects Withdrawn, n (%)	22 (2.1)		33 (1.6)		55 (1.8)	
Withdrawn due to Adverse Events, n (%)	2 (0.2)		9 (0.4)		11 (0.4)	
Withdrawn due to Lack of Efficacy, n (%)	Not applicable		Not applicable		Not applicable	
Withdrawn for other reasons, n (%)	20 (1.9)		24 (1.2)		44 (1.4)	
Demographics	50-64y		65y+		50y+	
N (Total Vaccinated Cohort)	1047		2007		3054	
Females:Males	599:448		1094:913		1693:1361	
Mean Age, years (SD)	57.6 (4.11)		70.3 (4.42)		65.9 (7.39)	
White - Caucasian / European heritage, n (%)	1015 (96.9)		1960 (97.7)		2975 (97.4)	
Primary Efficacy Results:						

Proportion of subjects with at least one ILI episode confirmed with viral culture and/or RT-PCR (influenza A and/or B infection) or not confirmed (Total Vaccinated Cohort)

		Age Groups											
		50-64y N = 297				65y+ N = 697				50y+ N = 994			
Germany													
	Event Type	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
ILI (confirmed or not)	At least 1 ILI episode	55	18.5	14.3	23.4	114	16.4	13.7	19.3	169	17.0	14.7	19.5
	1 ILI episode	50	16.8	12.8	21.6	105	15.1	12.5	17.9	155	15.6	13.4	18.0
	2 ILI episodes	5	1.7	0.5	3.9	9	1.3	0.6	2.4	14	1.4	0.8	2.4
	>2 ILI episodes	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Lab confirmed influenza (Viral culture and/or RT-PCR)	Influenza A and/or B	4	1.3	0.4	3.4	9	1.3	0.6	2.4	13	1.3	0.7	2.2
	Influenza A only#	4	1.3	0.4	3.4	9	1.3	0.6	2.4	13	1.3	0.7	2.2
	Influenza B only#	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
	Influenza A and B#	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Viral culture confirmed influenza	Influenza A and/or B	4	1.3	0.4	3.4	6	0.9	0.3	1.9	10	1.0	0.5	1.8
	Influenza A only#	4	1.3	0.4	3.4	6	0.9	0.3	1.9	10	1.0	0.5	1.8
	Influenza B only#	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
	Influenza A and B#	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
RT-PCR confirmed influenza	Influenza A and/or B	4	1.3	0.4	3.4	9	1.3	0.6	2.4	13	1.3	0.7	2.2
	Influenza A only#	4	1.3	0.4	3.4	9	1.3	0.6	2.4	13	1.3	0.7	2.2
	Influenza B only#	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
	Influenza A and B#	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Viral culture and RT-PCR confirmed influenza	Influenza A and/or B	4	1.3	0.4	3.4	6	0.9	0.3	1.9	10	1.0	0.5	1.8
	Influenza A only#	4	1.3	0.4	3.4	6	0.9	0.3	1.9	10	1.0	0.5	1.8
	Influenza B only#	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
	Influenza A and B#	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Netherlands													
ILI (confirmed or not)	At least 1 ILI episode	40	14.0	10.2	18.6	50	11.1	8.4	14.4	90	12.2	10.0	14.8
	1 ILI episode	38	13.3	9.6	17.8	48	10.7	8.0	13.9	86	11.7	9.5	14.2
	2 ILI episodes	2	0.7	0.1	2.5	2	0.4	0.1	1.6	4	0.5	0.1	1.4
	>2 ILI episodes	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
Lab confirmed influenza (Viral culture and/or RT-PCR)	Influenza A and/or B	3	1.0	0.2	3.0	2	0.4	0.1	1.6	5	0.7	0.2	1.6
	Influenza A only#	3	1.0	0.2	3.0	2	0.4	0.1	1.6	5	0.7	0.2	1.6
	Influenza B only#	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	Influenza A and B#	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
Viral culture confirmed influenza	Influenza A and/or B	3	1.0	0.2	3.0	0	0.0	0.0	0.8	3	0.4	0.1	1.2
	Influenza A only#	3	1.0	0.2	3.0	0	0.0	0.0	0.8	3	0.4	0.1	1.2
	Influenza B only#	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	Influenza A and B#	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
RT-PCR confirmed influenza	Influenza A and/or B	3	1.0	0.2	3.0	2	0.4	0.1	1.6	5	0.7	0.2	1.6
	Influenza A only#	3	1.0	0.2	3.0	2	0.4	0.1	1.6	5	0.7	0.2	1.6
	Influenza B only#	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	Influenza A and B#	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
Viral culture and RT-PCR confirmed influenza	Influenza A and/or B	3	1.0	0.2	3.0	0	0.0	0.0	0.8	3	0.4	0.1	1.2
	Influenza A only#	3	1.0	0.2	3.0	0	0.0	0.0	0.8	3	0.4	0.1	1.2
	Influenza B only#	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	Influenza A and B#	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
Poland													
ILI (confirmed or not)	At least 1 ILI episode	22	7.6	4.8	11.3	40	8.0	5.8	10.8	62	7.9	6.1	10.0
	1 ILI episode	21	7.2	4.5	10.9	39	7.8	5.6	10.6	60	7.6	5.9	9.7

	2 ILI episodes	1	0.3	0.0	1.9	1	0.2	0.0	1.1	2	0.3	0.0	0.9
	>2 ILI episodes	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Lab confirmed influenza (Viral culture and/or RT-PCR)	Influenza A and/or B	6	2.1	0.8	4.4	4	0.8	0.2	2.0	10	1.3	0.6	2.3
	Influenza A only#	6	2.1	0.8	4.4	4	0.8	0.2	2.0	10	1.3	0.6	2.3
	Influenza B only#	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Influenza A and B#	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Viral culture confirmed influenza	Influenza A and/or B	5	1.7	0.6	4.0	3	0.6	0.1	1.8	8	1.0	0.4	2.0
	Influenza A only#	5	1.7	0.6	4.0	3	0.6	0.1	1.8	8	1.0	0.4	2.0
	Influenza B only#	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Influenza A and B#	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
RT-PCR confirmed influenza	Influenza A and/or B	6	2.1	0.8	4.4	4	0.8	0.2	2.0	10	1.3	0.6	2.3
	Influenza A only#	6	2.1	0.8	4.4	4	0.8	0.2	2.0	10	1.3	0.6	2.3
	Influenza B only#	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Influenza A and B#	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Viral culture and RT-PCR confirmed influenza	Influenza A and/or B	5	1.7	0.6	4.0	3	0.6	0.1	1.8	8	1.0	0.4	2.0
	Influenza A only#	5	1.7	0.6	4.0	3	0.6	0.1	1.8	8	1.0	0.4	2.0
	Influenza B only#	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Influenza A and B#	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
United States													
ILI (confirmed or not)	At least 1 ILI episode	16	9.2	5.3	14.5	39	10.7	7.7	14.4	55	10.2	7.8	13.1
	1 ILI episode	16	9.2	5.3	14.5	39	10.7	7.7	14.4	55	10.2	7.8	13.1
	2 ILI episodes	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	>2 ILI episodes	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Lab confirmed influenza (Viral culture and/or RT-PCR)	Influenza A and/or B	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza A only#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza B only#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza A and B#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Viral culture confirmed influenza	Influenza A and/or B	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza A only#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza B only#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza A and B#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
RT-PCR confirmed influenza	Influenza A and/or B	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza A only#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza B only#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza A and B#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Viral culture and RT-PCR confirmed influenza	Influenza A and/or B	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza A only#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza B only#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Influenza A and B#	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Total													
ILI (confirmed or not)	At least 1 ILI episode	133	12.7	10.7	14.9	243	12.1	10.7	13.6	376	12.3	11.2	13.5
	1 ILI episode	125	11.9	10.0	14.1	231	11.5	10.1	13.0	356	11.7	10.5	12.8
	2 ILI episodes	8	0.8	0.3	1.5	12	0.6	0.3	1.0	20	0.7	0.4	1.0
	>2 ILI episodes	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
Lab confirmed influenza (Viral culture and/or RT-PCR)	Influenza A and/or B	13	1.2	0.7	2.1	15	0.7	0.4	1.2	28	0.9	0.6	1.3
	Influenza A only#	13	1.2	0.7	2.1	15	0.7	0.4	1.2	28	0.9	0.6	1.3
	Influenza B only#	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
	Influenza A and B#	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
Viral culture confirmed influenza	Influenza A and/or B	12	1.1	0.6	2.0	9	0.4	0.2	0.8	21	0.7	0.4	1.0
	Influenza A only#	12	1.1	0.6	2.0	9	0.4	0.2	0.8	21	0.7	0.4	1.0
	Influenza B only#	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
	Influenza A and B#	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1

RT-PCR confirmed influenza	Influenza A and/or B	13	1.2	0.7	2.1	15	0.7	0.4	1.2	28	0.9	0.6	1.3
	Influenza A only#	13	1.2	0.7	2.1	15	0.7	0.4	1.2	28	0.9	0.6	1.3
	Influenza B only#	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
	Influenza A and B#	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
Viral culture and RT-PCR confirmed influenza	Influenza A and/or B	12	1.1	0.6	2.0	9	0.4	0.2	0.8	21	0.7	0.4	1.0
	Influenza A only#	12	1.1	0.6	2.0	9	0.4	0.2	0.8	21	0.7	0.4	1.0
	Influenza B only#	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
	Influenza A and B#	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1

Only the first episode has been taken into account

N = total number of subjects

n (%) = number (percentage) of subjects with a specified event type

95% CI = Exact 95% confidence interval - LL = Lower Limit, UL = Upper Limit

Primary Efficacy Results:

Proportion of subjects with at least one pneumonia, ischemic Heart Disease (unstable angina or myocardial infarction), congestive heart failure, acute cerebrovascular disease (stroke or transient ischemic attack) or COPD exacerbation (Total vaccinated cohort)

		Age Groups											
		50-64y N = 297				65y+ N = 697				50y+ N = 994			
Germany													
		n	%	95% CI		n	%	95% CI		n	%	95% CI	
Illness	Number of Episodes			LL	UL			LL	UL			LL	UL
Pneumonia	At least one episode	0	0.0	0.0	1.2	4	0.6	0.2	1.5	4	0.4	0.1	1.0
	One episode	0	0.0	0.0	1.2	4	0.6	0.2	1.5	4	0.4	0.1	1.0
	Above one episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Ischemic heart disease	At least one episode	0	0.0	0.0	1.2	1	0.1	0.0	0.8	1	0.1	0.0	0.6
	One episode	0	0.0	0.0	1.2	1	0.1	0.0	0.8	1	0.1	0.0	0.6
	Above one episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Unstable angina	At least one episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
	One episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
	Above one episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Myocardial infarction	At least one episode	0	0.0	0.0	1.2	1	0.1	0.0	0.8	1	0.1	0.0	0.6
	One episode	0	0.0	0.0	1.2	1	0.1	0.0	0.8	1	0.1	0.0	0.6
	Above one episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Congestive heart failure	At least one episode	0	0.0	0.0	1.2	2	0.3	0.0	1.0	2	0.2	0.0	0.7
	One episode	0	0.0	0.0	1.2	2	0.3	0.0	1.0	2	0.2	0.0	0.7
	Above one episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Acute cerebrovascular disease	At least one episode	0	0.0	0.0	1.2	1	0.1	0.0	0.8	1	0.1	0.0	0.6
	One episode	0	0.0	0.0	1.2	1	0.1	0.0	0.8	1	0.1	0.0	0.6
	Above one episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Stroke	At least one episode	0	0.0	0.0	1.2	1	0.1	0.0	0.8	1	0.1	0.0	0.6
	One episode	0	0.0	0.0	1.2	1	0.1	0.0	0.8	1	0.1	0.0	0.6
	Above one episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Transient ischemic attack	At least one episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
	One episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
	Above one episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
COPD exacerbation	At least one episode	1	0.3	0.0	1.9	1	0.1	0.0	0.8	2	0.2	0.0	0.7
	One episode	1	0.3	0.0	1.9	1	0.1	0.0	0.8	2	0.2	0.0	0.7
	Above one episode	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Any illness*	At least one episode	1	0.3	0.0	1.9	8	1.1	0.5	2.2	9	0.9	0.4	1.7
	One episode	1	0.3	0.0	1.9	7	1.0	0.4	2.1	8	0.8	0.3	1.6
	Two episodes	0	0.0	0.0	1.2	1	0.1	0.0	0.8	1	0.1	0.0	0.6
Netherlands													
Pneumonia	At least one episode	1	0.3	0.0	1.9	4	0.9	0.2	2.3	5	0.7	0.2	1.6

	One episode	1	0.3	0.0	1.9	4	0.9	0.2	2.3	5	0.7	0.2	1.6
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	At least one episode	1	0.3	0.0	1.9	2	0.4	0.1	1.6	3	0.4	0.1	1.2
Ischemic heart disease	One episode	1	0.3	0.0	1.9	2	0.4	0.1	1.6	3	0.4	0.1	1.2
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
Unstable angina	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
Myocardial infarction	One episode	1	0.3	0.0	1.9	2	0.4	0.1	1.6	3	0.4	0.1	1.2
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	At least one episode	1	0.3	0.0	1.9	2	0.4	0.1	1.6	3	0.4	0.1	1.2
Congestive heart failure	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
Acute cerebrovascular disease	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
Stroke	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
Transient ischemic attack	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
COPD exacerbation	One episode	0	0.0	0.0	1.3	1	0.2	0.0	1.2	1	0.1	0.0	0.8
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	At least one episode	0	0.0	0.0	1.3	1	0.2	0.0	1.2	1	0.1	0.0	0.8
Any illness*	One episode	2	0.7	0.1	2.5	7	1.6	0.6	3.2	9	1.2	0.6	2.3
	Two episodes	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
	At least one episode	2	0.7	0.1	2.5	7	1.6	0.6	3.2	9	1.2	0.6	2.3
Poland													
Pneumonia	At least one episode	1	0.3	0.0	1.9	0	0.0	0.0	0.7	1	0.1	0.0	0.7
	One episode	1	0.3	0.0	1.9	0	0.0	0.0	0.7	1	0.1	0.0	0.7
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Ischemic heart disease	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Unstable angina	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Myocardial infarction	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Congestive heart failure	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Acute cerebrovascular disease	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Stroke	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Transient ischemic attack	At least one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5

COPD exacerbation	At least one episode	0	0.0	0.0	1.3	1	0.2	0.0	1.1	1	0.1	0.0	0.7
	One episode	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Above one episode	0	0.0	0.0	1.3	1	0.2	0.0	1.1	1	0.1	0.0	0.7
Any illness*	At least one episode	1	0.3	0.0	1.9	1	0.2	0.0	1.1	2	0.3	0.0	0.9
	One episode	1	0.3	0.0	1.9	0	0.0	0.0	0.7	1	0.1	0.0	0.7
	Two episodes	0	0.0	0.0	1.3	1	0.2	0.0	1.1	1	0.1	0.0	0.7
United States													
Pneumonia	At least one episode	0	0.0	0.0	2.1	1	0.3	0.0	1.5	1	0.2	0.0	1.0
	One episode	0	0.0	0.0	2.1	1	0.3	0.0	1.5	1	0.2	0.0	1.0
	Above one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Ischemic heart disease	At least one episode	1	0.6	0.0	3.2	0	0.0	0.0	1.0	1	0.2	0.0	1.0
	One episode	1	0.6	0.0	3.2	0	0.0	0.0	1.0	1	0.2	0.0	1.0
	Above one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Unstable angina	At least one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	One episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Above one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Myocardial infarction	At least one episode	1	0.6	0.0	3.2	0	0.0	0.0	1.0	1	0.2	0.0	1.0
	One episode	1	0.6	0.0	3.2	0	0.0	0.0	1.0	1	0.2	0.0	1.0
	Above one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Congestive heart failure	At least one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	One episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Above one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Acute cerebrovascular disease	At least one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	One episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Above one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Stroke	At least one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	One episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Above one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Transient ischemic attack	At least one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	One episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Above one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
COPD exacerbation	At least one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	One episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Above one episode	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Any illness*	At least one episode	1	0.6	0.0	3.2	1	0.3	0.0	1.5	2	0.4	0.0	1.3
	One episode	1	0.6	0.0	3.2	1	0.3	0.0	1.5	2	0.4	0.0	1.3
	Two episodes	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Total													
Pneumonia	At least one episode	2	0.2	0.0	0.7	9	0.4	0.2	0.8	11	0.4	0.2	0.6
	One episode	2	0.2	0.0	0.7	9	0.4	0.2	0.8	11	0.4	0.2	0.6
	Above one episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
Ischemic heart disease	At least one episode	2	0.2	0.0	0.7	3	0.1	0.0	0.4	5	0.2	0.1	0.4
	One episode	2	0.2	0.0	0.7	3	0.1	0.0	0.4	5	0.2	0.1	0.4
	Above one episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
Unstable angina	At least one episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
	One episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
	Above one episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
Myocardial infarction	At least one episode	2	0.2	0.0	0.7	3	0.1	0.0	0.4	5	0.2	0.1	0.4
	One episode	2	0.2	0.0	0.7	3	0.1	0.0	0.4	5	0.2	0.1	0.4
	Above one episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
Congestive heart failure	At least one episode	0	0.0	0.0	0.4	2	0.1	0.0	0.4	2	0.1	0.0	0.2
	One episode	0	0.0	0.0	0.4	2	0.1	0.0	0.4	2	0.1	0.0	0.2
	Above one episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
Acute cerebrovascular disease	At least one episode	0	0.0	0.0	0.4	1	0.05	0.0	0.3	1	0.03	0.0	0.2

Stroke	One episode	0	0.0	0.0	0.4	1	0.05	0.0	0.3	1	0.03	0.0	0.2
	Above one episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
	At least one episode	0	0.0	0.0	0.4	1	0.05	0.0	0.3	1	0.03	0.0	0.2
	One episode	0	0.0	0.0	0.4	1	0.05	0.0	0.3	1	0.03	0.0	0.2
Transient ischemic attack	Above one episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
	At least one episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
	One episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
	Above one episode	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
COPD exacerbation	At least one episode	1	0.1	0.0	0.5	3	0.1	0.0	0.4	4	0.1	0.0	0.3
	One episode	1	0.1	0.0	0.5	2	0.1	0.0	0.4	3	0.1	0.0	0.3
	Above one episode	0	0.0	0.0	0.4	1	0.05	0.0	0.3	1	0.03	0.0	0.2
	One episode	5	0.5	0.2	1.1	17	0.8	0.5	1.4	22	0.7	0.5	1.1
Any illness*	One episode	5	0.5	0.2	1.1	15	0.7	0.4	1.2	20	0.7	0.4	1.0
	Two episodes	0	0.0	0.0	0.4	2	0.1	0.0	0.4	2	0.1	0.0	0.2

N = total number of subjects

n/% = number/percentage of subjects with a specific number of illness episodes

95% CI = Exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

* The episodes of each illness were pooled. For example, a subject who reported one episode of pneumonia and one episode of myocardial infarction had 2 episodes for any illness.

Primary Efficacy Results:

Proportion of subjects with at least one hospitalization or emergency room visit or unscheduled medical office visit or unscheduled visit to GP due to any reason, due to ILI, due to laboratory confirmed influenza infection and due to pneumonia, ischemic Heart Disease or congestive heart failure or acute cerebrovascular disease or COPD exacerbation (Total vaccinated cohort)

		Age Groups											
		50-64y N = 297				65y+ N = 697				50y+ N = 994			
Germany													
Reason of hospitalization or emergency room visit	Number of hospitalization or ER visits	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
Any reason	At least one	23	7.7	5.0	11.4	68	9.8	7.7	12.2	91	9.2	7.4	11.1
	One	21	7.1	4.4	10.6	57	8.2	6.3	10.5	78	7.8	6.3	9.7
	Above one	2	0.7	0.1	2.4	11	1.6	0.8	2.8	13	1.3	0.7	2.2
ILI	At least one	15	5.1	2.9	8.2	24	3.4	2.2	5.1	39	3.9	2.8	5.3
	One	15	5.1	2.9	8.2	23	3.3	2.1	4.9	38	3.8	2.7	5.2
	Above one	0	0.0	0.0	1.2	1	0.1	0.0	0.8	1	0.1	0.0	0.6
Laboratory confirmed influenza infection	At least one	1	0.3	0.0	1.9	3	0.4	0.1	1.3	4	0.4	0.1	1.0
	One	1	0.3	0.0	1.9	3	0.4	0.1	1.3	4	0.4	0.1	1.0
	Above one	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4
Pneumonia, ischemic HD, congestive heart failure, acute cerebrovascular disease or COPD exacerbation	At least one	0	0.0	0.0	1.2	7	1.0	0.4	2.1	7	0.7	0.3	1.4
	One	0	0.0	0.0	1.2	6	0.9	0.3	1.9	6	0.6	0.2	1.3
	Above one	0	0.0	0.0	1.2	1	0.1	0.0	0.8	1	0.1	0.0	0.6
Other reason*	At least one	8	2.7	1.2	5.2	46	6.6	4.9	8.7	54	5.4	4.1	7.0
	One	6	2.0	0.7	4.3	43	6.2	4.5	8.2	49	4.9	3.7	6.5
	Above one	2	0.7	0.1	2.4	3	0.4	0.1	1.3	5	0.5	0.2	1.2
Netherlands													
Any reason	At least one	11	3.8	1.9	6.8	24	5.3	3.5	7.8	35	4.8	3.3	6.6
	One	9	3.1	1.4	5.9	20	4.5	2.7	6.8	29	3.9	2.7	5.6
	Above one	2	0.7	0.1	2.5	4	0.9	0.2	2.3	6	0.8	0.3	1.8
ILI	At least one	8	2.8	1.2	5.4	14	3.1	1.7	5.2	22	3.0	1.9	4.5
	One	8	2.8	1.2	5.4	14	3.1	1.7	5.2	22	3.0	1.9	4.5
	Above one	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5

Laboratory confirmed influenza infection	At least one	1	0.3	0.0	1.9	2	0.4	0.1	1.6	3	0.4	0.1	1.2
	One	1	0.3	0.0	1.9	2	0.4	0.1	1.6	3	0.4	0.1	1.2
	Above one	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
Pneumonia, ischemic HD, congestive heart failure, acute cerebrovascular disease or COPD exacerbation	At least one	2	0.7	0.1	2.5	7	1.6	0.6	3.2	9	1.2	0.6	2.3
	One	2	0.7	0.1	2.5	7	1.6	0.6	3.2	9	1.2	0.6	2.3
	Above one	0	0.0	0.0	1.3	0	0.0	0.0	0.8	0	0.0	0.0	0.5
Other reason*	At least one	2	0.7	0.1	2.5	9	2.0	0.9	3.8	11	1.5	0.7	2.7
	One	1	0.3	0.0	1.9	9	2.0	0.9	3.8	10	1.4	0.7	2.5
	Above one	1	0.3	0.0	1.9	0	0.0	0.0	0.8	1	0.1	0.0	0.8
Poland													
Any reason	At least one	8	2.8	1.2	5.4	20	4.0	2.5	6.1	28	3.6	2.4	5.1
	One	8	2.8	1.2	5.4	18	3.6	2.2	5.7	26	3.3	2.2	4.8
	Above one	0	0.0	0.0	1.3	2	0.4	0.0	1.4	2	0.3	0.0	0.9
ILI	At least one	4	1.4	0.4	3.5	9	1.8	0.8	3.4	13	1.7	0.9	2.8
	One	4	1.4	0.4	3.5	8	1.6	0.7	3.1	12	1.5	0.8	2.6
	Above one	0	0.0	0.0	1.3	1	0.2	0.0	1.1	1	0.1	0.0	0.7
Laboratory confirmed influenza infection	At least one	0	0.0	0.0	1.3	1	0.2	0.0	1.1	1	0.1	0.0	0.7
	One	0	0.0	0.0	1.3	1	0.2	0.0	1.1	1	0.1	0.0	0.7
	Above one	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Pneumonia, ischemic HD, congestive heart failure, acute cerebrovascular disease or COPD exacerbation	At least one	1	0.3	0.0	1.9	1	0.2	0.0	1.1	2	0.3	0.0	0.9
	One	1	0.3	0.0	1.9	0	0.0	0.0	0.7	1	0.1	0.0	0.7
	Above one	0	0.0	0.0	1.3	1	0.2	0.0	1.1	1	0.1	0.0	0.7
Other reason*	At least one	3	1.0	0.2	3.0	10	2.0	1.0	3.7	13	1.7	0.9	2.8
	One	3	1.0	0.2	3.0	10	2.0	1.0	3.7	13	1.7	0.9	2.8
	Above one	0	0.0	0.0	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.5
United States													
Any reason	At least one	5	2.9	0.9	6.6	12	3.3	1.7	5.7	17	3.2	1.9	5.0
	One	5	2.9	0.9	6.6	12	3.3	1.7	5.7	17	3.2	1.9	5.0
	Above one	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
ILI	At least one	4	2.3	0.6	5.8	4	1.1	0.3	2.8	8	1.5	0.6	2.9
	One	4	2.3	0.6	5.8	4	1.1	0.3	2.8	8	1.5	0.6	2.9
	Above one	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Laboratory confirmed influenza infection	At least one	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	One	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
	Above one	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Pneumonia, ischemic HD, congestive heart failure, acute cerebrovascular disease or COPD exacerbation	At least one	1	0.6	0.0	3.2	1	0.3	0.0	1.5	2	0.4	0.0	1.3
	One	1	0.6	0.0	3.2	1	0.3	0.0	1.5	2	0.4	0.0	1.3
	Above one	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Other reason*	At least one	0	0.0	0.0	2.1	7	1.9	0.8	3.9	7	1.3	0.5	2.7
	One	0	0.0	0.0	2.1	7	1.9	0.8	3.9	7	1.3	0.5	2.7
	Above one	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Total													
Any reason	At least one	47	4.5	3.3	5.9	124	6.2	5.2	7.3	171	5.6	4.8	6.5
	One	43	4.1	3.0	5.5	107	5.3	4.4	6.4	150	4.9	4.2	5.7
	Above one	4	0.4	0.1	1.0	17	0.8	0.5	1.4	21	0.7	0.4	1.0
ILI	At least one	31	3.0	2.0	4.2	51	2.5	1.9	3.3	82	2.7	2.1	3.3
	One	31	3.0	2.0	4.2	49	2.4	1.8	3.2	80	2.6	2.1	3.2
	Above one	0	0.0	0.0	0.4	2	0.1	0.0	0.4	2	0.1	0.0	0.2
Laboratory confirmed	At least one	2	0.2	0.0	0.7	6	0.3	0.1	0.6	8	0.3	0.1	0.5

influenza infection	One	2	0.2	0.0	0.7	6	0.3	0.1	0.6	8	0.3	0.1	0.5
	Above one	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
Pneumonia, ischemic HD, congestive heart failure, acute cerebrovascular disease or COPD exacerbation	At least one	4	0.4	0.1	1.0	16	0.8	0.5	1.3	20	0.7	0.4	1.0
	One	4	0.4	0.1	1.0	14	0.7	0.4	1.2	18	0.6	0.3	0.9
	Above one	0	0.0	0.0	0.4	2	0.1	0.0	0.4	2	0.1	0.0	0.2
Other reason*	At least one	13	1.2	0.7	2.1	72	3.6	2.8	4.5	85	2.8	2.2	3.4
	One	10	1.0	0.5	1.7	69	3.4	2.7	4.3	79	2.6	2.1	3.2
	Above one	3	0.3	0.1	0.8	3	0.1	0.0	0.4	6	0.2	0.1	0.4

N = total number of subjects

n (%) = number (percentage) of subjects with hospitalization or emergency room visit due to the specified reason

95% CI = Exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

ischemic HD = ischemic Heart Disease = unstable angina or myocardial infarction

acute cerebrovascular disease = stroke or transient ischemic attack

* = for hospitalization/emergency room visit only

Primary Efficacy Results:

Number of deaths during the influenza season (Total vaccinated cohort)

Cause of death #	GE												NL			
	50-64y N = 297				65y+ N = 697				50y+ N = 994				50-64y N = 286			
	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
Laboratory confirmed influenza infection	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4	0	0.0	0.0	1.3
ILI (not laboratory confirmed as influenza)	0	0.0	0.0	1.2	0	0.0	0.0	0.5	0	0.0	0.0	0.4	0	0.0	0.0	1.3
Other	0	0.0	0.0	1.2	5	0.7	0.2	1.7	5	0.5	0.2	1.2	0	0.0	0.0	1.3

	NL								PL							
	65y+ N = 449				50y+ N = 735				50-64y N = 290				65y+ N = 497			
	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
Laboratory confirmed influenza infection	0	0.0	0.0	0.8	0	0.0	0.0	0.5	0	0.0	0.0	1.3	0	0.0	0.0	0.7
ILI (not laboratory confirmed as influenza)	0	0.0	0.0	0.8	0	0.0	0.0	0.5	0	0.0	0.0	1.3	0	0.0	0.0	0.7
Other	1	0.2	0.0	1.2	1	0.1	0.0	0.8	0	0.0	0.0	1.3	0	0.0	0.0	0.7

	PL				US											
	50y+ N = 787				50-64y N = 174				65y+ N = 364				50y+ N = 538			
	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
Laboratory confirmed influenza infection	0	0.0	0.0	0.5	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
ILI (not laboratory confirmed as influenza)	0	0.0	0.0	0.5	0	0.0	0.0	2.1	0	0.0	0.0	1.0	0	0.0	0.0	0.7
Other	0	0.0	0.0	0.5	1	0.6	0.0	3.2	0	0.0	0.0	1.0	1	0.2	0.0	1.0

	Total											
	50-64y N = 1047				65y+ N = 2007				50y+ N = 3054			
	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
Laboratory confirmed influenza infection	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
ILI (not laboratory confirmed as influenza)	0	0.0	0.0	0.4	0	0.0	0.0	0.2	0	0.0	0.0	0.1
Other	1	0.1	0.0	0.5	6	0.3	0.1	0.6	7	0.2	0.1	0.5

N = total number of subjects

n (%) = number (percentage) of subjects with a specific event type
95%CI=Exact 95% confidence interval: LL = Lower limit, UL = upper limit
= Several causes of death could be counted for the same subject

Primary Efficacy Results:

Proportion of subjects with laboratory RT-PCR confirmed RSV infection (Total vaccinated cohort)

Country	50-64y N = 297				65y+ N = 697				50y+ N = 994			
			95% CI				95% CI				95% CI	
	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
Germany	5	1.7	0.5	3.9	12	1.7	0.9	3.0	17	1.7	1.0	2.7
Netherlands	6	2.1	0.8	4.5	7	1.6	0.6	3.2	13	1.8	0.9	3.0
Poland	2	0.7	0.1	2.5	4	0.8	0.2	2.0	6	0.8	0.3	1.7
United States	3	1.7	0.4	5.0	4	1.1	0.3	2.8	7	1.3	0.5	2.7
Total	16	1.5	0.9	2.5	27	1.3	0.9	2.0	43	1.4	1.0	1.9

N = total number of subjects

n (%) = number (percentage) of subjects with the specified event type

95%CI = Exact 95%confidence interval LL = lower limit UL = Upper limit

Primary Efficacy Results:

Seropositivity rates and GMTs for HI antibody titers at Day 0 and 21 (ATP cohort for immunogenicity)

					≥ 1:10				GMT		
							95% CI			95% CI	
Antibody	Country	Age	Timing	N	n	%	LL	UL	value	LL	UL
A/New Caledonia	GE	50-64y	PRE	52	51	98.1	89.7	100	42.7	31.2	58.4
			PI(D21)	52	52	100	93.2	100	178.1	129.1	245.6
		65y+	PRE	76	76	100	95.3	100	45.9	37.6	56.0
			PI(D21)	76	76	100	95.3	100	99.6	81.6	121.6
		50y+	PRE	128	127	99.2	95.7	100	44.6	37.5	52.9
			PI(D21)	128	128	100	97.2	100	126.1	105.3	151.1
	NL	50-64y	PRE	39	35	89.7	75.8	97.1	25.8	18.7	35.7
			PI(D21)	39	39	100	91.0	100	236.6	160.4	348.9
		65y+	PRE	78	76	97.4	91.0	99.7	73.2	57.5	93.1
			PI(D21)	78	77	98.7	93.1	100	128.1	100.9	162.7
		50y+	PRE	117	111	94.9	89.2	98.1	51.7	41.9	63.8
			PI(D21)	117	116	99.1	95.3	100	157.2	127.6	193.6
	PL	50-64y	PRE	41	39	95.1	83.5	99.4	45.4	29.1	70.7
			PI(D21)	41	41	100	91.4	100	234.0	158.2	346.1
		65y+	PRE	77	69	89.6	80.6	95.4	24.5	19.4	30.8
			PI(D21)	77	77	100	95.3	100	182.4	136.3	244.0
		50y+	PRE	118	108	91.5	85.0	95.9	30.3	24.4	37.7
			PI(D21)	118	118	100	96.9	100	198.9	157.8	250.6
	US	50-64y	PRE	39	37	94.9	82.7	99.4	52.6	34.5	80.2
			PI(D21)	39	39	100	91.0	100	236.4	160.8	347.6
		65y+	PRE	76	73	96.1	88.9	99.2	42.2	33.1	53.7
			PI(D21)	76	76	100	95.3	100	179.3	136.4	235.8
		50y+	PRE	115	110	95.7	90.1	98.6	45.5	36.8	56.2
			PI(D21)	115	115	100	96.8	100	197.0	157.9	245.7
	Total	50-64y	PRE	171	162	94.7	90.2	97.6	40.5	33.7	48.8
			PI(D21)	171	171	100	97.9	100	216.4	180.8	259.0
		65y+	PRE	307	294	95.8	92.9	97.7	43.2	38.3	48.7
			PI(D21)	307	306	99.7	98.2	100	142.9	125.8	162.4
		50y+	PRE	478	456	95.4	93.1	97.1	42.2	38.1	46.7
			PI(D21)	478	477	99.8	98.8	100	165.8	149.2	184.2
A/Wisconsin	GE	50-64y	PRE	52	33	63.5	49.0	76.4	20.5	13.4	31.6
			PI(D21)	52	51	98.1	89.7	100	153.6	101.4	232.7

B/Malaysia	NL	65y+	PRE	76	61	80.3	69.5	88.5	29.3	21.3	40.4
			PI(D21)	76	76	100	95.3	100	184.3	132.4	256.4
		50y+	PRE	128	94	73.4	64.9	80.9	25.4	19.6	32.8
			PI(D21)	128	127	99.2	95.7	100	171.2	132.6	221.0
		50-64y	PRE	39	17	43.6	27.8	60.4	13.6	9.0	20.7
			PI(D21)	39	37	94.9	82.7	99.4	136.3	87.9	211.2
		65y+	PRE	78	59	75.6	64.6	84.7	31.7	22.1	45.5
			PI(D21)	78	76	97.4	91.0	99.7	144.4	106.4	196.0
		50y+	PRE	117	76	65.0	55.6	73.5	24.0	18.0	31.8
			PI(D21)	117	113	96.6	91.5	99.1	141.7	110.7	181.3
	PL	50-64y	PRE	41	22	53.7	37.4	69.3	15.1	10.0	22.8
			PI(D21)	41	40	97.6	87.1	99.9	135.0	86.4	210.9
		65y+	PRE	77	35	45.5	34.1	57.2	10.7	8.5	13.4
			PI(D21)	77	77	100	95.3	100	182.3	135.6	245.0
		50y+	PRE	118	57	48.3	39.0	57.7	12.1	9.8	14.8
			PI(D21)	118	117	99.2	95.4	100	164.2	128.5	209.8
		50-64y	PRE	39	30	76.9	60.7	88.9	18.3	12.3	27.1
			PI(D21)	39	39	100	91.0	100	216.3	126.2	370.6
	US	65y+	PRE	76	54	71.1	59.5	80.9	21.7	15.9	29.6
			PI(D21)	76	75	98.7	92.9	100	213.4	159.7	285.2
		50y+	PRE	115	84	73.0	64.0	80.9	20.5	16.1	26.1
			PI(D21)	115	114	99.1	95.3	100	214.4	165.3	278.0
		50-64y	PRE	171	102	59.6	51.9	67.1	16.9	13.8	20.8
			PI(D21)	171	167	97.7	94.1	99.4	156.7	125.3	196.0
	Total	65y+	PRE	307	209	68.1	62.5	73.3	21.5	18.4	25.3
			PI(D21)	307	304	99.0	97.2	99.8	179.1	154.0	208.4
		50y+	PRE	478	311	65.1	60.6	69.3	19.8	17.4	22.4
			PI(D21)	478	471	98.5	97.0	99.4	170.8	150.6	193.6
	GE	50-64y	PRE	52	33	63.5	49.0	76.4	15.7	11.5	21.6
			PI(D21)	52	50	96.2	86.8	99.5	91.4	65.7	127.2
		65y+	PRE	76	66	86.8	77.1	93.5	33.0	25.3	43.0
			PI(D21)	76	75	98.7	92.9	100	130.8	99.4	172.1
		50y+	PRE	128	99	77.3	69.1	84.3	24.4	19.8	30.1
			PI(D21)	128	125	97.7	93.3	99.5	113.1	91.6	139.6
	NL	50-64y	PRE	39	33	84.6	69.5	94.1	24.8	17.7	34.7
			PI(D21)	39	39	100	91.0	100	194.6	138.2	274.1
		65y+	PRE	78	76	97.4	91.0	99.7	51.7	41.8	64.1
			PI(D21)	78	78	100	95.4	100	160.7	129.9	198.9
		50y+	PRE	117	109	93.2	87.0	97.0	40.5	33.5	49.0
			PI(D21)	117	117	100	96.9	100	171.3	143.1	205.1
	PL	50-64y	PRE	41	30	73.2	57.1	85.8	17.9	12.4	25.8
			PI(D21)	41	41	100	91.4	100	142.0	100.1	201.6
		65y+	PRE	77	61	79.2	68.5	87.6	19.8	15.6	25.2
			PI(D21)	77	77	100	95.3	100	165.9	126.8	217.0
		50y+	PRE	118	91	77.1	68.5	84.3	19.1	15.7	23.3
			PI(D21)	118	118	100	96.9	100	157.2	127.3	194.0
	US	50-64y	PRE	39	36	92.3	79.1	98.4	33.4	23.0	48.7
			PI(D21)	39	38	97.4	86.5	99.9	236.5	149.7	373.8
		65y+	PRE	76	74	97.4	90.8	99.7	67.2	52.3	86.3
			PI(D21)	76	76	100	95.3	100	330.5	261.9	417.1
		50y+	PRE	115	110	95.7	90.1	98.6	53.0	42.8	65.7
			PI(D21)	115	114	99.1	95.3	100	295.0	237.6	366.3
	Total	50-64y	PRE	171	132	77.2	70.2	83.3	21.4	18.0	25.4
			PI(D21)	171	168	98.2	95.0	99.6	149.9	124.3	180.9

	65y+	PRE	307	277	90.2	86.3	93.3	38.8	34.1	44.2
		PI(D21)	307	306	99.7	98.2	100	184.0	161.9	209.2
	50y+	PRE	478	409	85.6	82.1	88.6	31.3	28.2	34.9
		PI(D21)	478	474	99.2	97.9	99.8	171.0	153.8	190.2

GMT = geometric mean antibody titer calculated on all subjects

N = number of subjects with available results

n (%) = number (percentage) of seropositive subjects (HI titer \geq 1:10)

95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

PI(D21) = 21 days after vaccination

PRE = Pre-vaccination

Primary Efficacy Results:

Seroconversion rate (SCR) for HI antibody titer at Day 21 (ATP cohort for immunogenicity)

			SCR				
			N	n	%	95% CI	
Vaccine strain	Country	Age				LL	UL
A/New Caledonia	GE	50-64y	52	22	42.3	28.7	56.8
		65y+	76	15	19.7	11.5	30.5
		50y+	128	37	28.9	21.2	37.6
	NL	50-64y	39	24	61.5	44.6	76.6
		65y+	78	8	10.3	4.5	19.2
		50y+	117	32	27.4	19.5	36.4
	PL	50-64y	41	20	48.8	32.9	64.9
		65y+	77	41	53.2	41.5	64.7
		50y+	118	61	51.7	42.3	61.0
	US	50-64y	39	18	46.2	30.1	62.8
		65y+	76	29	38.2	27.2	50.0
		50y+	115	47	40.9	31.8	50.4
	Total	50-64y	171	84	49.1	41.4	56.9
		65y+	307	93	30.3	25.2	35.8
		50y+	478	177	37.0	32.7	41.5
A/Wisconsin	GE	50-64y	52	33	63.5	49.0	76.4
		65y+	76	45	59.2	47.3	70.4
		50y+	128	78	60.9	51.9	69.4
	NL	50-64y	39	28	71.8	55.1	85.0
		65y+	78	38	48.7	37.2	60.3
		50y+	117	66	56.4	46.9	65.6
	PL	50-64y	41	25	61.0	44.5	75.8
		65y+	77	61	79.2	68.5	87.6
		50y+	118	86	72.9	63.9	80.7
	US	50-64y	39	28	71.8	55.1	85.0
		65y+	76	53	69.7	58.1	79.8
		50y+	115	81	70.4	61.2	78.6
	Total	50-64y	171	114	66.7	59.1	73.7
		65y+	307	197	64.2	58.5	69.5
		50y+	478	311	65.1	60.6	69.3
B/Malaysia	GE	50-64y	52	26	50.0	35.8	64.2
		65y+	76	36	47.4	35.8	59.2
		50y+	128	62	48.4	39.5	57.4
	NL	50-64y	39	32	82.1	66.5	92.5
		65y+	78	30	38.5	27.7	50.2
		50y+	117	62	53.0	43.5	62.3
	PL	50-64y	41	27	65.9	49.4	79.9
		65y+	77	53	68.8	57.3	78.9
		50y+	118	80	67.8	58.6	76.1

	US	50-64y	39	22	56.4	39.6	72.2
		65y+	76	41	53.9	42.1	65.5
		50y+	115	63	54.8	45.2	64.1
	Total	50-64y	171	107	62.6	54.9	69.8
		65y+	307	160	52.1	46.4	57.8
		50y+	478	267	55.9	51.3	60.4

N = Number of subjects with available results at day 0 and day 21

n (%) = number (percentage) of subjects who seroconverted at day 21

95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Primary Efficacy Results:

Seroprotection rates (SPR) for HI antibody titers at Day 0 and 21 (ATP cohort for immunogenicity)

					SPR			
							95% CI	
Vaccine strain	Country	Age	Timing	N	n	%	LL	UL
A/New Caledonia	GE	50-64y	PRE	52	30	57.7	43.2	71.3
			PI(D21)	52	48	92.3	81.5	97.9
		65y+	PRE	76	50	65.8	54.0	76.3
			PI(D21)	76	72	94.7	87.1	98.5
		50y+	PRE	128	80	62.5	53.5	70.9
			PI(D21)	128	120	93.8	88.1	97.3
	NL	50-64y	PRE	39	16	41.0	25.6	57.9
			PI(D21)	39	38	97.4	86.5	99.9
		65y+	PRE	78	65	83.3	73.2	90.8
			PI(D21)	78	73	93.6	85.7	97.9
		50y+	PRE	117	81	69.2	60.0	77.4
			PI(D21)	117	111	94.9	89.2	98.1
	PL	50-64y	PRE	41	23	56.1	39.7	71.5
			PI(D21)	41	39	95.1	83.5	99.4
		65y+	PRE	77	29	37.7	26.9	49.4
			PI(D21)	77	76	98.7	93.0	100
		50y+	PRE	118	52	44.1	34.9	53.5
			PI(D21)	118	115	97.5	92.7	99.5
	US	50-64y	PRE	39	22	56.4	39.6	72.2
			PI(D21)	39	36	92.3	79.1	98.4
		65y+	PRE	76	40	52.6	40.8	64.2
			PI(D21)	76	73	96.1	88.9	99.2
		50y+	PRE	115	62	53.9	44.4	63.2
			PI(D21)	115	109	94.8	89.0	98.1
	Total	50-64y	PRE	171	91	53.2	45.4	60.9
			PI(D21)	171	161	94.2	89.5	97.2
		65y+	PRE	307	184	59.9	54.2	65.5
			PI(D21)	307	294	95.8	92.9	97.7
		50y+	PRE	478	275	57.5	53.0	62.0
			PI(D21)	478	455	95.2	92.9	96.9
A/Wisconsin	GE	50-64y	PRE	52	16	30.8	18.7	45.1
			PI(D21)	52	44	84.6	71.9	93.1
		65y+	PRE	76	31	40.8	29.6	52.7
			PI(D21)	76	68	89.5	80.3	95.3
		50y+	PRE	128	47	36.7	28.4	45.7
			PI(D21)	128	112	87.5	80.5	92.7
	NL	50-64y	PRE	39	11	28.2	15.0	44.9
			PI(D21)	39	34	87.2	72.6	95.7
		65y+	PRE	78	37	47.4	36.0	59.1
			PI(D21)	78	70	89.7	80.8	95.5

		50y+	PRE	117	48	41.0	32.0	50.5
			PI(D21)	117	104	88.9	81.7	93.9
	PL	50-64y	PRE	41	11	26.8	14.2	42.9
			PI(D21)	41	33	80.5	65.1	91.2
		65y+	PRE	77	13	16.9	9.3	27.1
			PI(D21)	77	70	90.9	82.2	96.3
		50y+	PRE	118	24	20.3	13.5	28.7
			PI(D21)	118	103	87.3	79.9	92.7
	US	50-64y	PRE	39	10	25.6	13.0	42.1
			PI(D21)	39	33	84.6	69.5	94.1
		65y+	PRE	76	25	32.9	22.5	44.6
			PI(D21)	76	72	94.7	87.1	98.5
		50y+	PRE	115	35	30.4	22.2	39.7
			PI(D21)	115	105	91.3	84.6	95.8
	Total	50-64y	PRE	171	48	28.1	21.5	35.4
			PI(D21)	171	144	84.2	77.9	89.3
		65y+	PRE	307	106	34.5	29.2	40.1
			PI(D21)	307	280	91.2	87.5	94.1
		50y+	PRE	478	154	32.2	28.0	36.6
			PI(D21)	478	424	88.7	85.5	91.4
B/Malaysia	GE	50-64y	PRE	52	16	30.8	18.7	45.1
			PI(D21)	52	44	84.6	71.9	93.1
		65y+	PRE	76	37	48.7	37.0	60.4
			PI(D21)	76	66	86.8	77.1	93.5
		50y+	PRE	128	53	41.4	32.8	50.4
			PI(D21)	128	110	85.9	78.7	91.4
	NL	50-64y	PRE	39	18	46.2	30.1	62.8
			PI(D21)	39	39	100	91.0	100
		65y+	PRE	78	60	76.9	66.0	85.7
			PI(D21)	78	76	97.4	91.0	99.7
		50y+	PRE	117	78	66.7	57.4	75.1
			PI(D21)	117	115	98.3	94.0	99.8
	PL	50-64y	PRE	41	11	26.8	14.2	42.9
			PI(D21)	41	36	87.8	73.8	95.9
		65y+	PRE	77	22	28.6	18.8	40.0
			PI(D21)	77	72	93.5	85.5	97.9
		50y+	PRE	118	33	28.0	20.1	37.0
			PI(D21)	118	108	91.5	85.0	95.9
	US	50-64y	PRE	39	18	46.2	30.1	62.8
			PI(D21)	39	36	92.3	79.1	98.4
		65y+	PRE	76	54	71.1	59.5	80.9
			PI(D21)	76	76	100	95.3	100
		50y+	PRE	115	72	62.6	53.1	71.5
			PI(D21)	115	112	97.4	92.6	99.5
	Total	50-64y	PRE	171	63	36.8	29.6	44.5
			PI(D21)	171	155	90.6	85.3	94.6
		65y+	PRE	307	173	56.4	50.6	62.0
			PI(D21)	307	290	94.5	91.3	96.7
		50y+	PRE	478	236	49.4	44.8	54.0
			PI(D21)	478	445	93.1	90.4	95.2

N = Number of subjects with available results
 n (%) = number (percentage) of seroprotected subjects (HI titer $\geq 1:40$)
 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
 PRE= Pre-vaccination

PI(D21)= 21 days after vaccination

Primary Efficacy Results:

Seroconversion factor (SCF) for HI antibody titer at Day 21 (ATP cohort for immunogenicity)

				SCF		
					95% CI	
Vaccine strain	Country	Age	N	Value	LL	UL
A/New Caledonia	GE	50-64y	52	4.2	2.7	6.3
		65y+	76	2.2	1.8	2.7
		50y+	128	2.8	2.3	3.5
	NL	50-64y	39	9.2	5.3	15.8
		65y+	78	1.8	1.5	2.1
		50y+	117	3.0	2.3	3.9
	PL	50-64y	41	5.2	3.2	8.4
		65y+	77	7.5	5.1	10.9
		50y+	118	6.6	4.9	8.8
	US	50-64y	39	4.5	2.7	7.5
		65y+	76	4.3	3.0	6.0
		50y+	115	4.3	3.3	5.7
	Total	50-64y	171	5.3	4.2	6.8
		65y+	307	3.3	2.8	3.9
		50y+	478	3.9	3.4	4.5
A/Wisconsin	GE	50-64y	52	7.5	4.6	12.1
		65y+	76	6.3	4.5	8.8
		50y+	128	6.7	5.1	8.9
	NL	50-64y	39	10.0	6.4	15.6
		65y+	78	4.6	3.4	6.0
		50y+	117	5.9	4.6	7.6
	PL	50-64y	41	8.9	5.7	14.0
		65y+	77	17.1	12.4	23.5
		50y+	118	13.6	10.5	17.7
	US	50-64y	39	11.8	6.9	20.3
		65y+	76	9.8	7.0	13.8
		50y+	115	10.5	7.9	13.9
	Total	50-64y	171	9.3	7.3	11.7
		65y+	307	8.3	7.0	9.8
		50y+	478	8.6	7.5	9.9
B/Malaysia	GE	50-64y	52	5.8	3.9	8.7
		65y+	76	4.0	3.0	5.3
		50y+	128	4.6	3.7	5.9
	NL	50-64y	39	7.9	6.0	10.4
		65y+	78	3.1	2.5	3.9
		50y+	117	4.2	3.5	5.1
	PL	50-64y	41	7.9	5.3	12.0
		65y+	77	8.4	6.1	11.4
		50y+	118	8.2	6.4	10.5
	US	50-64y	39	7.1	4.1	12.1
		65y+	76	4.9	3.7	6.5
		50y+	115	5.6	4.3	7.2
	Total	50-64y	171	7.0	5.7	8.6
		65y+	307	4.7	4.1	5.5
		50y+	478	5.5	4.8	6.1

N = Number of subjects with pre- and post-vaccination results available

SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])

95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s): Not Applicable**Safety Results:** Number (%) of subjects with unsolicited adverse events (Total vaccinated cohort)

Unsolicited AEs following vaccination were not collected.

Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) during the entire study period (Total vaccinated cohort)

All SAEs	Germany			Netherlands		
	50-64y N = 297	65y+ N = 697	50y+ N = 994	50-64y N = 286	65y+ N = 449	50y+ N = 735
Subjects with any SAE(s), n (%) [n related]	12 (4.04) [0]	57 (8.18) [0]	69 (6.94) [0]	3 (1.05) [0]	13 (2.90) [0]	16 (2.18) [0]
Myocardial infarction	1 (0.34) [0]	1 (0.14) [0]	2 (0.20) [0]	1 (0.35) [0]	2 (0.45) [0]	3 (0.41) [0]
Angina pectoris	0 (0.00) [0]	3 (0.43) [0]	3 (0.30) [0]	0 (0.00) [0]	2 (0.45) [0]	2 (0.27) [0]
Pneumonia	0 (0.00) [0]	4 (0.57) [0]	4 (0.40) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Atrial fibrillation	0 (0.00) [0]	2 (0.29) [0]	2 (0.20) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Coronary artery disease	0 (0.00) [0]	4 (0.57) [0]	4 (0.40) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Angina unstable	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac arrest	1 (0.34) [0]	1 (0.14) [0]	2 (0.20) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Cerebrovascular accident	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Abdominal abscess	1 (0.34) [0]	1 (0.14) [0]	2 (0.20) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Anaemia	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Arrhythmia	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Chest pain	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cholelithiasis	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Chronic obstructive pulmonary disease	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Gastritis	1 (0.34) [0]	0 (0.00) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Helicobacter gastritis	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Hypoacusis	1 (0.34) [0]	0 (0.00) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Lung neoplasm	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Osteoarthritis	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pancreatic carcinoma	0 (0.00) [0]	2 (0.29) [0]	2 (0.20) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Prostate cancer	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Psoriasis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.35) [0]	1 (0.22) [0]	2 (0.27) [0]
Abscess	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Acute coronary syndrome	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Acute myocardial infarction	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Anal fistula	1 (0.34) [0]	0 (0.00) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Aortic aneurysm	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Appendicitis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Arterial occlusive disease	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Arterial stenosis limb	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Arteriosclerosis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Atrial flutter	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Atrioventricular block	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Atrioventricular block first degree	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Bacteraemia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Bladder neoplasm	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Bleeding varicose vein	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Bone pain	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Breast cancer	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Bronchitis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Bronchitis chronic	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac failure	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac failure acute	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac failure congestive	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac pacemaker malfunction	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Carotid artery stenosis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]

Chronic sinusitis	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Colonic polyp	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Concussion	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Coronary artery occlusion	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Death	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Dislocation of joint prosthesis	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Diverticulitis	1 (0.34) [0]	0 (0.00) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Face injury	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Femoral arterial stenosis	1 (0.34) [0]	0 (0.00) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Femoral artery occlusion	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Femur fracture	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Gastric ulcer	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Gastroenteritis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Gastrointestinal carcinoma	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Gastrooesophageal reflux disease	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.35) [0]	0 (0.00) [0]	1 (0.14) [0]
Haematemesis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Head injury	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Heart rate increased	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Hepatic cirrhosis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Hiatus hernia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Hiccups	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Hypersensitivity	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Hypertension	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Inguinal hernia	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Intervertebral disc protrusion	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Ischaemia	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Lumbar spinal stenosis	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Lung adenocarcinoma	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Malignant melanoma	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Meniscus lesion	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Multiple fractures	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Nasal polyps	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Oesophageal carcinoma	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Oesophagitis	1 (0.34) [0]	0 (0.00) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Organ failure	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pain in extremity	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pancreatitis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Pancreatitis acute	1 (0.34) [0]	0 (0.00) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pleural effusion	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pleuritic pain	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Post-traumatic pain	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Postmenopausal haemorrhage	1 (0.34) [0]	0 (0.00) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Prostatic adenoma	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Prostatomegaly	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Pulmonary embolism	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pyrexia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Radial nerve palsy	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Radius fracture	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Rectal cancer	1 (0.34) [0]	0 (0.00) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Rectal polyp	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Retinal artery occlusion	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Retinitis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Sepsis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Shock	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Small intestinal obstruction	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Spinal column stenosis	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]

Staphylococcal sepsis	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Syncope	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Tachycardia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Tendon rupture	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Thrombophlebitis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Transient ischaemic attack	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Umbilical hernia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Upper respiratory tract infection	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Urinary incontinence	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Urinary retention	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Uterine leiomyoma	1 (0.34) [0]	0 (0.00) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Vascular graft occlusion	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Vertigo	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Vestibular disorder	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Vitreous haemorrhage	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Fatal SAES	50-64y N = 297	65y+ N = 697	50y+ N = 994	50-64y N = 286	65y+ N = 449	50y+ N = 735
subjects with fatal sae(s), n (%) [n related]	0 (0.00) [0]	8 (1.15) [0]	8 (0.80) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Cardiac arrest	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	1 (0.22) [0]	1 (0.14) [0]
Pancreatic carcinoma	0 (0.00) [0]	2 (0.29) [0]	2 (0.20) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac failure	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac failure acute	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cerebrovascular accident	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Death	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Hepatic cirrhosis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Lung adenocarcinoma	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Organ failure	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pulmonary embolism	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Sepsis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Shock	0 (0.00) [0]	1 (0.14) [0]	1 (0.10) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
	Poland			United States		
All SAEs	50-64y N = 290	65y+ N = 497	50y+ N = 787	50-64y N = 174	65y+ N = 364	50y+ N = 538
Subjects with any SAE(s), n (%) [n related]	2 (0.69) [0]	18 (3.62) [0]	20 (2.54) [0]	6 (3.45) [0]	17 (4.67) [0]	23 (4.28) [0]
Myocardial infarction	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Angina pectoris	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pneumonia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Atrial fibrillation	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	2 (0.55) [0]	2 (0.37) [0]
Coronary artery disease	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Angina unstable	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	1 (0.57) [0]	1 (0.27) [0]	2 (0.37) [0]
Cardiac arrest	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cerebrovascular accident	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.57) [0]	1 (0.27) [0]	2 (0.37) [0]
Abdominal abscess	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Anaemia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Arrhythmia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Chest pain	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	2 (0.55) [0]	2 (0.37) [0]
Cholelithiasis	1 (0.34) [0]	0 (0.00) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Chronic obstructive pulmonary disease	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.57) [0]	0 (0.00) [0]	1 (0.19) [0]
Gastritis	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Helicobacter gastritis	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Hypoacusis	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Lung neoplasm	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Osteoarthritis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Pancreatic carcinoma	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Prostate cancer	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	2 (0.55) [0]	2 (0.37) [0]

Psoriasis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Abscess	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Acute coronary syndrome	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Acute myocardial infarction	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.57) [0]	0 (0.00) [0]	1 (0.19) [0]
Anal fistula	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Aortic aneurysm	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Appendicitis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Arterial occlusive disease	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Arterial stenosis limb	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Arteriosclerosis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Atrial flutter	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.57) [0]	0 (0.00) [0]	1 (0.19) [0]
Atrioventricular block	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Atrioventricular block first degree	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Bacteraemia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.57) [0]	0 (0.00) [0]	1 (0.19) [0]
Bladder neoplasm	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Bleeding varicose vein	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Bone pain	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Breast cancer	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Bronchitis	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Bronchitis chronic	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac failure	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac failure acute	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac failure congestive	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Cardiac pacemaker malfunction	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Carotid artery stenosis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Chronic sinusitis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Colonic polyp	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Concussion	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Coronary artery occlusion	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Death	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Dislocation of joint prosthesis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Diverticulitis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Face injury	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Femoral arterial stenosis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Femoral artery occlusion	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Femur fracture	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Gastric ulcer	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Gastroenteritis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Gastrointestinal carcinoma	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Gastrooesophageal reflux disease	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Haematemesis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Head injury	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Heart rate increased	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Hepatic cirrhosis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.57) [0]	0 (0.00) [0]	1 (0.19) [0]
Hiatus hernia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Hiccups	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Hypersensitivity	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Hypertension	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Inguinal hernia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Intervertebral disc protrusion	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Ischaemia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Lumbar spinal stenosis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Lung adenocarcinoma	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Malignant melanoma	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Meniscus lesion	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Multiple fractures	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]

Nasal polyps	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Oesophageal carcinoma	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Oesophagitis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Organ failure	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pain in extremity	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pancreatitis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pancreatitis acute	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pleural effusion	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pleuritic pain	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Post-traumatic pain	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Postmenopausal haemorrhage	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Prostatic adenoma	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Prostatomegaly	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pulmonary embolism	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pyrexia	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Radial nerve palsy	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Radius fracture	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Rectal cancer	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Rectal polyp	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Retinal artery occlusion	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Retinitis	1 (0.34) [0]	0 (0.00) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Sepsis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.57) [0]	0 (0.00) [0]	1 (0.19) [0]
Shock	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Small intestinal obstruction	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Spinal column stenosis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Staphylococcal sepsis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Syncope	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Tachycardia	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.27) [0]	1 (0.19) [0]
Tendon rupture	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Thrombophlebitis	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Transient ischaemic attack	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Umbilical hernia	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Upper respiratory tract infection	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Urinary incontinence	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Urinary retention	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Uterine leiomyoma	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Vascular graft occlusion	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Vertigo	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Vestibular disorder	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Vitreous haemorrhage	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Fatal SAES	50-64y N = 290	65y+ N = 497	50y+ N = 787	50-64y N = 174	65y+ N = 364	50y+ N = 538
subjects with fatal sae(s), n (%) [n related]	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	2 (1.15) [0]	0 (0.00) [0]	2 (0.37) [0]
Cardiac arrest	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pancreatic carcinoma	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac failure	0 (0.00) [0]	1 (0.20) [0]	1 (0.13) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cardiac failure acute	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Cerebrovascular accident	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.57) [0]	0 (0.00) [0]	1 (0.19) [0]
Death	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Hepatic cirrhosis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.57) [0]	0 (0.00) [0]	1 (0.19) [0]
Lung adenocarcinoma	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Organ failure	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Pulmonary embolism	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Sepsis	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	1 (0.57) [0]	0 (0.00) [0]	1 (0.19) [0]
Shock	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]	0 (0.00) [0]
Total						

All SAEs	50-64y N = 1047	65y+ N = 2007	50y+ N = 3054
Subjects with any SAE(s), n (%) [n related]	23 (2.20) [0]	105 (5.23) [0]	128 (4.19) [0]
Myocardial infarction	2 (0.19) [0]	4 (0.20) [0]	6 (0.20) [0]
Angina pectoris	0 (0.00) [0]	5 (0.25) [0]	5 (0.16) [0]
Pneumonia	0 (0.00) [0]	5 (0.25) [0]	5 (0.16) [0]
Atrial fibrillation	0 (0.00) [0]	4 (0.20) [0]	4 (0.13) [0]
Coronary artery disease	0 (0.00) [0]	4 (0.20) [0]	4 (0.13) [0]
Angina unstable	1 (0.10) [0]	2 (0.10) [0]	3 (0.10) [0]
Cardiac arrest	1 (0.10) [0]	2 (0.10) [0]	3 (0.10) [0]
Cerebrovascular accident	1 (0.10) [0]	2 (0.10) [0]	3 (0.10) [0]
Abdominal abscess	1 (0.10) [0]	1 (0.05) [0]	2 (0.07) [0]
Anaemia	0 (0.00) [0]	2 (0.10) [0]	2 (0.07) [0]
Arrhythmia	0 (0.00) [0]	2 (0.10) [0]	2 (0.07) [0]
Chest pain	0 (0.00) [0]	2 (0.10) [0]	2 (0.07) [0]
Cholelithiasis	1 (0.10) [0]	1 (0.05) [0]	2 (0.07) [0]
Chronic obstructive pulmonary disease	1 (0.10) [0]	1 (0.05) [0]	2 (0.07) [0]
Gastritis	1 (0.10) [0]	1 (0.05) [0]	2 (0.07) [0]
Helicobacter gastritis	0 (0.00) [0]	2 (0.10) [0]	2 (0.07) [0]
Hypoacusis	1 (0.10) [0]	1 (0.05) [0]	2 (0.07) [0]
Lung neoplasm	0 (0.00) [0]	2 (0.10) [0]	2 (0.07) [0]
Osteoarthritis	0 (0.00) [0]	2 (0.10) [0]	2 (0.07) [0]
Pancreatic carcinoma	0 (0.00) [0]	2 (0.10) [0]	2 (0.07) [0]
Prostate cancer	0 (0.00) [0]	2 (0.10) [0]	2 (0.07) [0]
Psoriasis	1 (0.10) [0]	1 (0.05) [0]	2 (0.07) [0]
Abscess	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Acute coronary syndrome	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Acute myocardial infarction	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Anal fistula	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Aortic aneurysm	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Appendicitis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Arterial occlusive disease	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Arterial stenosis limb	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Arteriosclerosis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Atrial flutter	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Atrioventricular block	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Atrioventricular block first degree	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Bacteraemia	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Bladder neoplasm	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Bleeding varicose vein	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Bone pain	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Breast cancer	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Bronchitis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Bronchitis chronic	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Cardiac failure	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Cardiac failure acute	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Cardiac failure congestive	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Cardiac pacemaker malfunction	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Carotid artery stenosis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Chronic sinusitis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Colonic polyp	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Concussion	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Coronary artery occlusion	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Death	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Dislocation of joint prosthesis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Diverticulitis	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]

Face injury	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Femoral arterial stenosis	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Femoral artery occlusion	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Femur fracture	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Gastric ulcer	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Gastroenteritis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Gastrointestinal carcinoma	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Gastrooesophageal reflux disease	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Haematemesis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Head injury	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Heart rate increased	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Hepatic cirrhosis	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Hiatus hernia	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Hiccups	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Hypersensitivity	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Hypertension	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Inguinal hernia	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Intervertebral disc protrusion	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Ischaemia	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Lumbar spinal stenosis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Lung adenocarcinoma	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Malignant melanoma	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Meniscus lesion	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Multiple fractures	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Nasal polyps	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Oesophageal carcinoma	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Oesophagitis	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Organ failure	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Pain in extremity	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Pancreatitis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Pancreatitis acute	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Pleural effusion	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Pleuritic pain	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Post-traumatic pain	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Postmenopausal haemorrhage	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Prostatic adenoma	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Prostatomegaly	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Pulmonary embolism	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Pyrexia	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Radial nerve palsy	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Radius fracture	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Rectal cancer	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Rectal polyp	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Retinal artery occlusion	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Retinitis	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Sepsis	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Shock	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Small intestinal obstruction	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Spinal column stenosis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Staphylococcal sepsis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Syncope	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Tachycardia	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Tendon rupture	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Thrombophlebitis	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Transient ischaemic attack	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Umbilical hernia	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]

Upper respiratory tract infection	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Urinary incontinence	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Urinary retention	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Uterine leiomyoma	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Vascular graft occlusion	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Vertigo	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Vestibular disorder	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Vitreous haemorrhage	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Fatal SAEs	50-64y N = 1047	65y+ N = 2007	50y+ N = 3054
Subjects with fatal SAE(s), n (%) [n related]	2 (0.19) [0]	10 (0.50) [0]	12 (0.39) [0]
Cardiac arrest	0 (0.00) [0]	2 (0.10) [0]	2 (0.07) [0]
Pancreatic carcinoma	0 (0.00) [0]	2 (0.10) [0]	2 (0.07) [0]
Cardiac failure	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Cardiac failure acute	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Cerebrovascular accident	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Death	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Hepatic cirrhosis	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Lung adenocarcinoma	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Organ failure	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Pulmonary embolism	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]
Sepsis	1 (0.10) [0]	0 (0.00) [0]	1 (0.03) [0]
Shock	0 (0.00) [0]	1 (0.05) [0]	1 (0.03) [0]

Conclusion: During the course of the study and across all countries, at least one ILI episode was reported for 133 (12.7%), 243 (12.1%) and 376 (12.3%) subjects in the 50-64y, 65y+ and 50y+ age groups, respectively; laboratory confirmed influenza (A and/or B) was reported for 13 (1.2%), 15 (0.7%) and 28 (0.9%) subjects in those same age groups, respectively; finally, at least one episode of any illness was reported for 5 (0.5%), 17 (0.8%) and 22 (0.7%) subjects in those 3 age groups, respectively. At Day 21 after vaccination, at least 94.2%, 84.2% and 90.6% of subjects had seroprotection rates (HI antibody titers $\geq 1:40$) for A/New Caledonia, A/Wisconsin and B/Malaysia strains, respectively. SAEs were reported for 23 (2.2%), 105 (5.2%) and 128 (4.2%) subjects in the 50-64y, 65y+ and 50y+ age groups, respectively. Fatal SAEs, of which none were influenza-related, were reported for 2, 10 and 12 subjects in the 50-64y, 65y+ and 50y+ age groups, respectively. None of the reported SAEs were considered by the investigators as related to the study vaccination.

Date updated: 11-August-2014