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.: 580299/012 (HPV-012) – 107476 (Ext M18) – 107477 (Ext M24) – 107479 (Ext M36) - 107481 (Ext M48)
Title: 580299/012 (HPV-012): A phase III, double-blind, randomized study to assess the consistency of the immunogenicity of three consecutive production lots of GlaxoSmithKline Biologicals' HPV-16/18 L1/AS04 vaccine administered intramuscularly according to a 0, 1, 6-month schedule in healthy female subjects aged 10 – 25 years and to demonstrate non-inferiority of the candidate HPV vaccine manufactured using different production processes. Extension studies: A long-term, open, follow-up of the immunogenicity and safety of GlaxoSmithKline Biologicals' HPV-16/18 L1 VLP AS04 vaccine in healthy female subjects vaccinated either pre- or post-menarche in the HPV-012 study. HPV-16/18 L1/AS04 vaccine: GlaxoSmithKline Biologicals' virus-like particle (VLP) vaccine against human papillomaviruses (HPV) 16/18
Rationale: The aim of the primary study was to compare the immunogenicity of 3 consecutive industrial production lots (80 L scale) of the HPV-16/18 VLP/AS04 vaccine in 15 to 25-year old women. The study also aimed at demonstrating the non-inferiority in terms of immunogenicity of the HPV vaccine manufactured with the new production process. In addition, the immunogenicity of the HPV vaccine produced at industrial scale was compared with the immune response induced in subjects from study 580299/001 (HPV-001). The aim of the extension studies was to assess the persistence of vaccine-induced immune responses against HPV-16/18 and long-term vaccine safety in subjects vaccinated either pre- or post-menarche and to compare anti-HPV-16 and anti-HPV-18 antibody levels in cervical samples with antibody levels in serum samples in subjects vaccinated pre- and post-menarche. In this document, HPV_new refers to the vaccine produced at industrial scale (new manufacturing process) while HPV_old refers to the vaccine produced with the old manufacturing process. Note: In the primary study, visits 1 to 4 corresponded to months 0, 1, 6 and 7 in the schedule; a telephone contact was foreseen at Month 12. In the extension studies, visits 5 to 8 corresponded to months 18, 24, 36 and 48 in the schedule. Only 8 subjects came to Visit 5 at Month 18 whereas most of the subjects came to Visit 6 at Month 24. As a consequence, no separate analysis at Month 18 was prepared; the data for Month 18 outcome variables were incorporated into the Month 24 analyses.
Phase: III
Study Period: 580299/012: 05 September 2004 to 15 July 2005 107476 (Ext M18): 27 June 2006 to 01 July 2006 107477 (Ext M24): 01 September 2006 to 21 December 2006 107479 (Ext M 36): 15 August 2007 to 21 December 2007 107481 (Ext M48): 21 August 2008 to 06 January 2009
Study Design: Partially double-blind, randomized (1:1:1:1:1) study with 5 parallel groups. This study was double-blind for subjects aged 15 to 25 years and single-blind for subjects aged 10 to 14 years.
Centers: 580299/012 (HPV-012): 17 centers (2 in Denmark, 2 in Estonia, 2 in Finland, 4 in Greece, 2 in the Netherlands and 5 in Russia) 107476 (Ext M18): 1 centre in Estonia 107477 (Ext M24), 107479 (Ext M 36) and 107481 (Ext M48): 6 centers (2 in Denmark, 2 in Estonia and 2 in Finland)
Indication: Active immunization of women from the age of 10 years onwards to prevent persistent HPV-16 & HPV-18 infection and HPV-16 & HPV-18 associated cervical neoplasia.
Treatment: The study groups were as follows: • Lot 1 Group: women aged 15 to 25 years received Lot 1 of HPV_new; • Lot 2 Group: women aged 15 to 25 years received Lot 2 of HPV_new; • Lot 3 Group: women aged 15 to 25 years received Lot 3 of HPV_new; • Old_M Group: women aged 15 to 25 years received HPV_old; • [10-14] Group: pre-teen and adolescent women (aged 10-14 years) received Lot 1 of HPV_new. All vaccines were administered intramuscularly into the deltoid of the non-dominant arm according to a 0, 1, 6-month schedule.

Objectives:

Primary study:

- To demonstrate lot-to-lot consistency in terms of immunogenicity between 3 different industrial production lots (80 L scale) of the HPV-16/18 L1/AS04 vaccine.
  The lot-lot consistency was demonstrated if, 1 month after the third dose, the two sided 90 % confidence interval (CI) of the geometric mean titer (GMT) ratio was within [0.5, 2].
  If lot-to-lot consistency was demonstrated, the 3 lots were pooled and non-inferiority of HPV_new versus HPV_old was evaluated as a second primary objective. (If consistency was not demonstrated, non-inferiority could not be tested).
- To demonstrate that HPV_new was non-inferior in terms of immunogenicity to HPV_old.
  Two criteria for non-inferiority were assessed sequentially (if the first one was not demonstrated, the second one could not be tested):
  (1) one month after the third dose, the difference between the percentage of subjects who seroconverted after administration of HPV_old versus the pooled lots of HPV_new was below 10%;
  (2) one month after the third dose, GMT ratio between HPV_old and pooled lots of HPV_new was below 2.

Extension studies:

To evaluate the long-term immunogenicity of the HPV-16/18 L1 VLP AS04 vaccine in all subjects who received the 3 vaccine doses and completed Visit 4 (Month 7) by enzyme-linked immunosorbent assay (ELISA) at each time point (Months 18, 24, 36 and 48).

Primary Outcome/Efficacy Variable:

Primary study:

- Anti-HPV-16/18 seroconversion rates and antibody titers for the 3 consecutive lots of HPV_new assessed by ELISA at Month 7.
- Anti-HPV-16/18 seroconversion rates and antibody titers for HPV_old vaccine assessed by ELISA at Month 7.

Seropositivity was defined as anti-HPV-16 titer $\geq$ 8 EU/mL and anti-HPV-18 titer $\geq$ 7 EU/mL.

Seroconversion was defined as the appearance of antibodies (i.e. anti-HPV-16 titer $\geq$ 8 EU/mL and anti-HPV-18 titer $\geq$ 7 EU/mL) in the serum of initially seronegative subjects.

Extension studies:

- Anti-HPV-16 and anti-HPV-18 antibody titers assessed by ELISA in all subjects at each time point (Months 18‡, 24, 36 and 48).

‡ Note: not all subjects attended Month 18 Visit; hence not all samples were available at this time point.

Secondary Outcome/Efficacy Variable(s):

Primary study:

Immunogenicity

- Anti-HPV-16/18 seroconversion rates and antibody titers in adult women aged 15-25 years and in pre-teen and adolescent women aged 10-14 years receiving the same lot (Lot 1) of HPV_new vaccine, assessed by ELISA at Month 7.
- Anti-HPV-16/18 seroconversion rates and antibody titers in adult women aged 15-25 years receiving in this study the HPV_new vaccine and in a pre-specified subset of subjects* randomly selected from the efficacy study 580299/001 (HPV-001) assessed by ELISA at Month 7.

**The analysis was performed on all subjects of the Total Vaccinated Cohort from the HPV-001 study rather than a pre-specified subset of subjects randomly selected from that study.*

Safety

- Occurrence, intensity and relationship to vaccination of solicited general symptoms, and occurrence and intensity of solicited local symptoms within 7 days (Day 0-6) after each and any vaccination.
- Occurrence, intensity and causal relationship to vaccination of unsolicited symptoms within 30 days (Day 0-29) after any vaccination.
- Occurrence and relationship to vaccination of serious adverse events (SAEs) throughout the study period (up to Month 7).
- Occurrence of new onset chronic diseases (NOCDs) and other medically significant conditions prompting emergency room visits or physician visits that were not related to common diseases throughout the study period (up to Month 7) regardless of causal relationship to vaccination and intensity.
- Occurrence of SAEs, NOCDs and other medically significant conditions up to Month 12 (extended safety follow-up).

Extension studies:

- Occurrence of pregnancies, SAEs, NOCDs and other medically significant conditions (i.e. adverse events (AEs) prompting emergency room or physician visits that are not (1) related to common diseases or (2) routine visits for

physical examination or vaccination, or SAEs that are not related to common diseases) throughout the study period (including the period from last contact of the primary HPV-012 study until the Visit 5 (Month 18) of the Ext HPV-012 study or Visit 6 (Month 24) for those subjects who missed Visit 5.

- Anti-HPV-16 and anti-HPV-18 antibody titers assessed by ELISA at each time point (Months 0, 7, 18, 24, 36 and 48).
- Anti-HPV-16 and anti-HPV-18 antibody titers from subjects enrolled in studies HPV-001/HPV-007 subjects assessed by ELISA at each time point[$]
- Anti-HPV-16 and anti-HPV-18 antibody titers in cervical samples (CVS) at Months 24, 36 and 48 in post-menarcheal subjects who volunteered for the procedure.
- Total IgG[£] evaluation in blood samples at Months 24, 36 and 48.
- Total IgG[£] evaluation in cervical samples at Months 24, 36 and 48 in the subset of subjects who had cervical samples collected.

[$]The kinetics of HPV-16 and HPV-18 antibody response as compared to the level of natural infection and the level of serologic plateau phase during the HPV-007 efficacy study was performed.
[£] The results for total IgG are not available.

Statistical Methods:
Analyses were performed on the Total Vaccinated Cohort, on the According-to-Protocol (ATP) Cohort for immunogenicity and on the Extended Safety Follow-Up (ESFU) Vaccinated Cohort.
- The Total Vaccinated Cohort included all vaccinated subjects for whom data were available at the considered time points, including those of the extension studies
- The ATP Cohort for 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 and who were not seropositive for both HPV antigens) for whom immunogenicity data were available at the considered time points, including those of the extension studies.
- The ESFU Vaccinated Cohort included all vaccinated subjects for whom data were available at Month 12, i.e., subjects that could be contacted by telephone for the primary study safety follow-up.

Primary study
Analysis of Immunogenicity
Descriptive analysis:
Analysis was performed on the ATP Cohort for immunogenicity and on the Total Vaccinated Cohort.
The analysis of immunogenicity was performed on initially seronegative subjects only (subjects seropositive for one antigen were eliminated for the analysis of that antigen but were still evaluable for the analysis of the other antigen).
For HPV-16 and HPV-18 IgG antibodies, for all groups and for the pooled lots group, the percentage of subjects who seroconverted was tabulated with their exact 95% Confidence Interval (CI) and the Geometric Mean Titers (GMTs) were tabulated together with their 95% CIs. Antibody titers below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculations.
For the comparison of the immunogenicity results with the study 580299/001 (HPV-001), sera from the subjects in the Total Vaccinated Cohorts were used.
Inferential analysis
The first primary objective of consistency was reached if the asymptotic two-sided 90% CIs for the ratio of anti-HPV-16/18 GMTs at Month 7 between each pair of HPV_new lots were all within the range [0.5, 2].
If lot to lot consistency was demonstrated, the different Lot groups were pooled into the Pooled_lots Group.
The second primary objective of non-inferiority was reached if the upper limit of the standardized asymptotic two-sided 95% CI for the difference between the percentage of subjects who seroconverted at Month 7 after administration of HPV_old versus the pooled lots was < 10% and the upper limit of the asymptotic two-sided 95% CI for the ratio of anti-HPV-16/18 GMTs at Month 7 between the Old_M Group and the Pooled_lots Group was < 2.
Analysis of safety
Analyses were performed on the Total Vaccinated Cohort.
For each solicited local and general symptom, the percentage of subjects with the symptom reported during the 7-day (Day 0-6) follow-up period was tabulated with exact 95% CI, by dose and across doses. The same tabulations were done for Grade 3 local and general solicited symptoms, and for general solicited symptoms which were assessed as related to the study vaccination. The percentage of subjects with unsolicited adverse events (AEs) during the 30-day (Day 0-29) follow-up period was summarized according to the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms. The percentage of subjects with at least one NOCD classified by the MedDRA preferred term and reported up to Month 7 regardless of causal relationship to vaccination and intensity was tabulated with exact 95% CI. The same tabulation was done for other medically significant conditions reported up to Month 7. The occurrence of SAEs up to Month 7 was tabulated according to MedDRA preferred terms.

Follow-up at Month 12

Analysis of safety

Analyses were performed on the ESFU Vaccinated Cohort.

The proportion of subjects with at least one report of NOCD classified by MedDRA preferred terms, during the extended safety follow-up (Month 7 to Month 12) regardless of causal relationship to vaccination and intensity was tabulated with exact 95% CI. The same tabulation was done for other medically significant conditions. The occurrence of SAEs during the extended safety follow-up (Month 7 to Month 12) was tabulated according to MedDRA preferred terms.

Extension studies at Month 24, Month 36 and Month 48.

Analysis of safety

The analyses were based on the Total Vaccinated Cohort.

The proportion of subjects with at least one report of NOCD classified by MedDRA preferred terms, during the extended safety follow-up (Months 12 to 24, Months 24 to 36 and Months 36 to 48) was tabulated with exact 95% CI. The same tabulation was done for other medically significant conditions. Pregnancies and their outcomes were tabulated. The occurrence of SAEs during the follow-up period was tabulated according to MedDRA preferred terms.

Analysis of immunogenicity

The analyses were based on the Total Vaccinated Cohort and on the ATP Cohort for immunogenicity.

For HPV-16 and HPV-18 IgG antibodies, in all groups, the percentage with exact 95% CI of seropositive subjects from the ATP Cohort for immunogenicity was tabulated and the GMTs with 95% CIs were tabulated by pre-vaccination status.

When a cervical sample result was available in post-menarcheal subjects from the Total Vaccinated Cohort, who had volunteered for this procedure, GMT with 95% CI and seropositivity with exact 95% CI in cervical samples were tabulated for antibodies for anti-HPV-16 and anti-HPV-18 assessed by ELISA.

Also the GMT with 95% CI and seropositivity with exact 95% CI in serum samples from the subjects having CVS samples results available were tabulated for anti-HPV-16 and HPV-18 IgG antibodies assessed by ELISA.

Study Population: Healthy adolescent and young adult women between the ages of 10 and 25 years were enrolled in the primary study. If of childbearing potential, subjects had to be abstinent or to have used adequate contraceptive precautions for 30 days prior to vaccination and to agree to continue such precautions for 2 months after completion of vaccination series. Subjects who reached menarche during the study had to agree to follow the same precautions. Subjects had to have had no more than 6 lifetime sexual partners prior to enrolment (this criterion may not have been applicable in subjects less than 18 years of age, depending on local regulatory/ethical requirements). Prior to the performance of any study-specific procedures, written informed consent was obtained from each subject or from a parent/guardian in the case of subjects below the age of consent (written assent was obtained from these subjects).

To be eligible for the HPV-012 extension studies, the subjects had to have participated in the HPV-012 primary study in Denmark, Estonia or Finland, and to have received 3 doses of vaccine and completed Visit 4 (Month 7). They had to sign the written informed consent prior to enrolment. For subjects below the legal age of consent, written informed consent had to be obtained from a parent or legally acceptable representative (LAR) and, in addition, the subject had to sign and personally date a written informed assent.

Number of subjects	Lot 1 Group	Lot 2 Group	Lot 3 Group
Planned, N	150	150	150
Randomized, N (Total Vaccinated Cohort)	156	156	146
Completed to Month 7, n (%)	148 (94.9)	149 (95.5)	145 (99.3)
Total Number Subjects Withdrawn, n (%)	8 (5.1)	7 (4.5)	1 (0.7)
Withdrawn due to Adverse Events, n (%)	1 (0.6)	2 (1.3)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	7 (4.5)	5 (3.2)	1 (0.7)
Demographics	Lot 1 Group	Lot 2 Group	Lot 3 Group
N (Total Vaccinated Cohort)	156	156	146
Females:Males	156:0	156:0	146:0
Mean Age, years (SD)	20.3 (2.83)	20.3 (2.92)	19.8 (3.12)
White/Caucasian, n (%)	150 (96.2)	152 (97.4)	139 (95.2)
Number of subjects	Pooled_lots Group	Old_M Group	[10-14] Group
Planned, N	450	150	150
Randomized, N (Total Vaccinated Cohort)	458	154	158
Completed to Month 7, n (%)	442 (96.5)	147 (95.5)	153 (96.8)
Total Number Subjects Withdrawn, n (%)	16 (3.5)	7 (4.5)	5 (3.2)
Withdrawn due to Adverse Events, n (%)	3 (0.7)	1 (0.6)	1 (0.6)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable

Withdrawn for other reasons, n (%)	13 (2.8)	6 (3.9)	4 (2.5)
Demographics	Pooled_lots Group	Old_M Group	[10-14] Group
N (Total Vaccinated Cohort)	458	154	158
Females:Males	458:0	154:0	158:0
Mean Age, years (SD)	20.2 (2.96)	20.3 (2.99)	12.4 (1.37)
White/Caucasian, n (%)	441 (96.3)	150 (97.4)	150 (94.9)

Primary Efficacy Results:
Ratios of post-vaccination anti-HPV-16 and anti-HPV-18 GMT at Month 7 between the 3 vaccine lots produced at industrial scale with their 90% CIs in initially seronegative subjects (ATP Cohort for immunogenicity)

Antibody	Group	N	GMT (EU/mL)	Group	N	GMT (EU/mL)	GMT ratio			
							Ratio order	Value	90% CI	
									LL	UL
HPV-16 IgG	Lot 1	118	7438.9	Lot 2	122	7150.3	Lot 1/ Lot 2	1.04	0.85*	1.27*
	Lot 1	118	7438.9	Lot 3	119	7297.2	Lot 1/ Lot 3	1.02	0.84*	1.24*
	Lot 2	122	7150.3	Lot 3	119	7297.2	Lot 2/ Lot 3	0.98	0.80*	1.19*
HPV-18 IgG	Lot 1	116	3070.1	Lot 2	126	3173.4	Lot 1/ Lot 2	0.97	0.80*	1.17*
	Lot 1	116	3070.1	Lot 3	122	3743.3	Lot 1/ Lot 3	0.82	0.68*	1.00*
	Lot 2	126	3173.4	Lot 3	122	3743.3	Lot 2/ Lot 3	0.85	0.70*	1.02*

N = Number of subjects with available results
90% CI = 90% asymptotic confidence interval; LL = lower limit, UL = upper limit
* Primary objective of lot-to-lot consistency was demonstrated since the 90%CIs were within the interval [0.5,2]

Primary Efficacy Results:
Non-inferiority assessment between Old_M Group and the Pooled_lots Group for anti-HPV-16 IgG and anti-HPV-18 IgG at Month 7 in initially seronegative subjects (ATP Cohort for immunogenicity)

Antibody	Group				Difference in seroconversion rate (Old_M minus Pooled_lots)		
	Old_M		Pooled_lots		%	95% CI	
	N	%	N	%		LL	UL
HPV-16 IgG	111	100	359	100	0.00	-3.35	1.06*
HPV-18 IgG	117	100	364	100	0.00	-3.18	1.04*

N = number of subjects with available results
% = percentage of subjects with HPV-16 IgG titer ≥ 8 EU/mL / HPV-18 IgG titer ≥ 7 EU/mL
95% CI = 95% Standardized asymptotic confidence interval; LL = lower limit, UL = upper limit
* The second primary objective was demonstrated since the UL of the 95% CI for the difference were below 10%.

Primary Efficacy Results:
Ratios of post-vaccination anti-HPV-16 and anti-HPV-18 GMT at Month 7 between the pooled vaccine lots and Old_M group with their 95% CIs in initially seronegative subjects (ATP Cohort for immunogenicity)

Antibody	Group				GMT ratio (Old_M / Pooled_lots)		
	Old_M		Pooled_lots		Value	95% CI	
	N	GMT (EU/mL)	N	GMT (EU/mL)		LL	UL
HPV-16 IgG	111	9595.5	359	7292.9	1.32	1.08	1.61*
HPV-18 IgG	117	4164.7	364	3318.8	1.25	1.04	1.51*

N = number of subjects with available results
95% CI = 95% asymptotic confidence interval; LL = lower limit, UL = upper limit
* The second primary objective was demonstrated since the UL of the 95% CIs were below 2.

Primary Efficacy Results:
Seroconversion rates and GMTs for HPV-16 IgG antibodies in initially seronegative subjects (ATP Cohort for immunogenicity)

Group	Timing	N	≥ 8 EU/mL				GMT (EU/mL)		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
Lot 1	PIII(M7)	118	118	100	96.9	100	7438.9	6324.6	8749.6
Lot 2	PIII(M7)	122	122	100	97.0	100	7150.3	6038.1	8467.3
Lot 3	PIII(M7)	119	119	100	96.9	100	7297.2	6136.8	8677.0
Pooled_lots	PIII(M7)	359	359	100	99.0	100	7292.9	6623.7	8029.7

Old_M	PIII(M7)	111	111	100	96.7	100	9595.5	8027.4	11469.9
[10-14]	PIII(M7)	143	143	100	97.5	100	17272.5	15117.9	19734.1

N = number of subjects with results available
n(%) = number(percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PIII(M7) = Post Dose III (Month 7)

Primary Efficacy Results:
Seroconversion rates and GMTs for HPV-18 IgG antibodies in initially seronegative subjects (ATP Cohort for immunogenicity)

Group	Timing	N	≥ 7 EU/mL				GMT (EU/mL)		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
Lot 1	PIII(M7)	116	116	100	96.9	100	3070.1	2600.0	3625.4
Lot 2	PIII(M7)	126	126	100	97.1	100	3173.4	2714.3	3710.2
Lot 3	PIII(M7)	122	122	100	97.0	100	3743.3	3173.3	4415.7
Pooled_lots	PIII(M7)	364	364	100	99.0	100	3318.8	3023.1	3643.5
Old_M	PIII(M7)	117	117	100	96.9	100	4164.7	3552.0	4882.9
[10-14]	PIII(M7)	141	141	100	97.4	100	6863.8	5976.3	7883.0

N = number of subjects with results available
n(%) = number(percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PIII(M7) = Post Dose III (Month 7)

Primary Efficacy Results:
Seropositivity rates and GMTs for HPV-16 IgG antibodies by pre-vaccination status (ATP Cohort for immunogenicity)

Group	Pre-Vacc Status	Timing	N	≥ 8 EU/mL				GMT (EU/mL)		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
Pooled_lots	S-	PRE	141	0	0.0	0.0	2.6	4.0	4.0	4.0
		PIII(M7)	141	141	100	97.4	100	7399.3	6379.1	8582.6
		PIII (M24)	141	141	100	97.4	100	1469.9	1266.2	1706.2
		PIII(M36)	132	132	100	97.2	100	1392.9	1194.0	1624.8
		PIII(M48)	123	123	100	97.0	100	1186.2	1007.4	1396.8
	S+	PRE	19	19	100	82.4	100	28.9	17.4	48.0
		PIII(M7)	19	19	100	82.4	100	4031.5	2493.2	6519.1
		PIII (M24)	19	19	100	82.4	100	1239.2	751.8	2042.5
		PIII(M36)	18	18	100	81.5	100	1432.3	858.0	2391.1
		PIII(M48)	18	18	100	81.5	100	874.7	501.5	1525.4
	Total	PRE	160	19	11.9	7.3	17.9	5.1	4.5	5.7
		PIII(M7)	160	160	100	97.7	100	6884.5	5961.2	7950.7
		PIII (M24)	160	160	100	97.7	100	1440.4	1249.3	1660.7
		PIII(M36)	150	150	100	97.6	100	1397.5	1207.1	1618.1
		PIII(M48)	141	141	100	97.4	100	1140.9	974.9	1335.3
Old_M	S-	PRE	43	0	0.0	0.0	8.2	4.0	4.0	4.0
		PIII(M7)	43	43	100	91.8	100	10091.4	7385.6	13788.4
		PIII (M24)	43	43	100	91.8	100	2012.2	1439.9	2812.1
		PIII(M36)	39	39	100	91.0	100	1771.5	1258.1	2494.4
		PIII(M48)	43	43	100	91.8	100	1543.8	1101.1	2164.6
	S+	PRE	8	8	100	63.1	100	137.9	40.2	473.5
		PIII(M7)	8	8	100	63.1	100	3912.9	2160.9	7085.5
		PIII (M24)	8	8	100	63.1	100	1413.0	512.7	3893.8
		PIII(M36)	7	7	100	59.0	100	1246.6	350.2	4437.6
		PIII(M48)	6	6	100	54.1	100	813.0	184.3	3585.9
	Total	PRE	51	8	15.7	7.0	28.6	7.0	4.7	10.4
		PIII(M7)	51	51	100	93.0	100	8697.8	6514.8	11612.4
		PIII (M24)	51	51	100	93.0	100	1903.7	1396.0	2596.0

		PIII(M36)	46	46	100	92.3	100	1679.3	1211.5	2327.6
		PIII(M48)	49	49	100	92.7	100	1427.3	1027.6	1982.4
[10-14]	S-	PRE	55	0	0.0	0.0	6.5	4.0	4.0	4.0
		PIII(M7)	55	55	100	93.5	100	20444.0	16333.6	25588.8
		PIII(M18)	7	7	100	59.0	100	2118.0	790.8	5672.5
		PIII (M24)	55	55	100	93.5	100	3861.7	2947.0	5060.4
		PIII(M36)	52	52	100	93.2	100	3353.0	2553.4	4403.1
		PIII(M48)	49	49	100	92.7	100	2862.2	2129.3	3847.3
	Total	PRE	55	0	0.0	0.0	6.5	4.0	4.0	4.0
		PIII(M7)	55	55	100	93.5	100	20444.0	16333.6	25588.8
		PIII(M18)	7	7	100	59.0	100	2118.0	790.8	5672.5
		PIII (M24)	55	55	100	93.5	100	3861.7	2947.0	5060.4
		PIII(M36)	52	52	100	93.2	100	3353.0	2553.4	4403.1
		PIII(M48)	49	49	100	92.7	100	2862.2	2129.3	3847.3

N = number of subjects with results available
n(%) = number(percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PIII(M7) = Post Dose III (Month 7)
PIII(M18) = Post Dose III (Month 18)
PIII(M24) = Post Dose III (Month 24)
PIII(M36) = Post Dose III (Month 36)
PIII(M48) = Post Dose III (Month 48)

Primary Efficacy Results:
Seropositivity rates and GMTs for HPV-18 IgG antibodies by pre-vaccination status (ATP Cohort for immunogenicity)

Group	Pre-Vacc Status	Timing	N	≥ 7 EU/mL				GMT (EU/mL)		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
Pooled_lots	S-	PRE	140	0	0.0	0.0	2.6	3.5	3.5	3.5
		PIII(M7)	140	140	100	97.4	100	3306.9	2864.3	3817.9
		PIII (M24)	140	140	100	97.4	100	636.3	540.8	748.7
		PIII(M36)	133	133	100	97.3	100	586.6	496.7	692.8
		PIII(M48)	123	123	100	97.0	100	469.8	394.7	559.2
	S+	PRE	20	20	100	83.2	100	39.1	21.7	70.2
		PIII(M7)	20	20	100	83.2	100	2393.9	1524.1	3760.1
		PIII (M24)	20	20	100	83.2	100	752.9	407.6	1390.6
		PIII(M36)	18	18	100	81.5	100	493.4	280.1	869.2
		PIII(M48)	18	18	100	81.5	100	414.6	231.4	742.8
	Total	PRE	160	20	12.5	7.8	18.6	4.7	4.1	5.5
		PIII(M7)	160	160	100	97.7	100	3176.0	2769.6	3642.1
		PIII (M24)	160	160	100	97.7	100	649.8	554.3	761.8
		PIII(M36)	151	151	100	97.6	100	574.7	490.2	673.7
		PIII(M48)	141	141	100	97.4	100	462.4	391.5	546.1
Old_M	S-	PRE	47	0	0.0	0.0	7.5	3.5	3.5	3.5
		PIII(M7)	47	47	100	92.5	100	4210.9	3267.0	5427.6
		PIII (M24)	47	47	100	92.5	100	764.3	557.3	1048.1
		PIII(M36)	42	42	100	91.6	100	631.3	441.9	901.9
		PIII(M48)	46	46	100	92.3	100	502.8	358.0	706.1
	S+	PRE	3	3	100	29.2	100	22.8	2.9	178.5
		PIII(M7)	3	3	100	29.2	100	4084.4	716.3	23287.8
		PIII (M24)	3	3	100	29.2	100	1045.6	185.3	5899.5
		PIII(M36)	3	3	100	29.2	100	968.2	241.7	3878.4
		PIII(M48)	2	2	100	15.8	100	1123.1	16.3	77306.2
	Total	PRE	50	3	6.0	1.3	16.5	3.9	3.4	4.5
		PIII(M7)	50	50	100	92.9	100	4203.2	3301.7	5350.9
		PIII (M24)	50	50	100	92.9	100	778.8	577.1	1050.8

		PIII(M36)	45	45	100	92.1	100	649.6	464.5	908.4
		PIII(M48)	48	48	100	92.6	100	519.9	374.1	722.4
[10-14]	S-	PRE	52	0	0.0	0.0	6.8	3.5	3.5	3.5
		PIII(M7)	52	52	100	93.2	100	8001.4	6340.8	10097.0
		PIII(M18)	7	7	100	59.0	100	990.3	399.0	2457.9
		PIII (M24)	52	52	100	93.2	100	1341.1	1044.4	1722.1
		PIII(M36)	49	49	100	92.7	100	1122.7	848.9	1484.9
		PIII(M48)	46	46	100	92.3	100	940.8	714.8	1238.3
	S+	PRE	2	2	100	15.8	100	8.5	4.0	17.9
		PIII(M7)	2	2	100	15.8	100	5174.6	4.3	6201326
		PIII (M24)	2	2	100	15.8	100	1360.5	1.4	1337388
		PIII(M36)	2	2	100	15.8	100	859.7	5.0	149083.1
		PIII(M48)	2	2	100	15.8	100	824.7	0.9	758371.6
	Total	PRE	54	2	3.7	0.5	12.7	3.6	3.5	3.8
		PIII(M7)	54	54	100	93.4	100	7873.3	6275.7	9877.7
		PIII(M18)	7	7	100	59.0	100	990.3	399.0	2457.9
		PIII (M24)	54	54	100	93.4	100	1341.8	1053.2	1709.6
		PIII(M36)	51	51	100	93.0	100	1111.0	848.5	1454.9
		PIII(M48)	48	48	100	92.6	100	935.6	717.9	1219.5

N = number of subjects with results available
n(%) = number(percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PIII(M7) = Post Dose III (Month 7)
PIII(M18) = Post Dose III (Month 18)
PIII(M24) = Post Dose III (Month 24)
PIII(M36) = Post Dose III (Month 36)
PIII(M48) = Post Dose III (Month 48)

Secondary Outcome Variable (s):
Seroconversion rates and GMTs for HPV-16 IgG antibodies at Month 7 (Total Vaccinated Cohort)

Group	N	≥ 8 EU/mL				GMT (EU/mL)		
		n	%	95% CI		value	95% CI	
				LL	UL		LL	UL
HPV-001	339	339	100	98.9	100	4415.9	3976.7	4903.6
Pooled_lots	368	368	100	99.0	100	7380.8	6712.0	8116.3

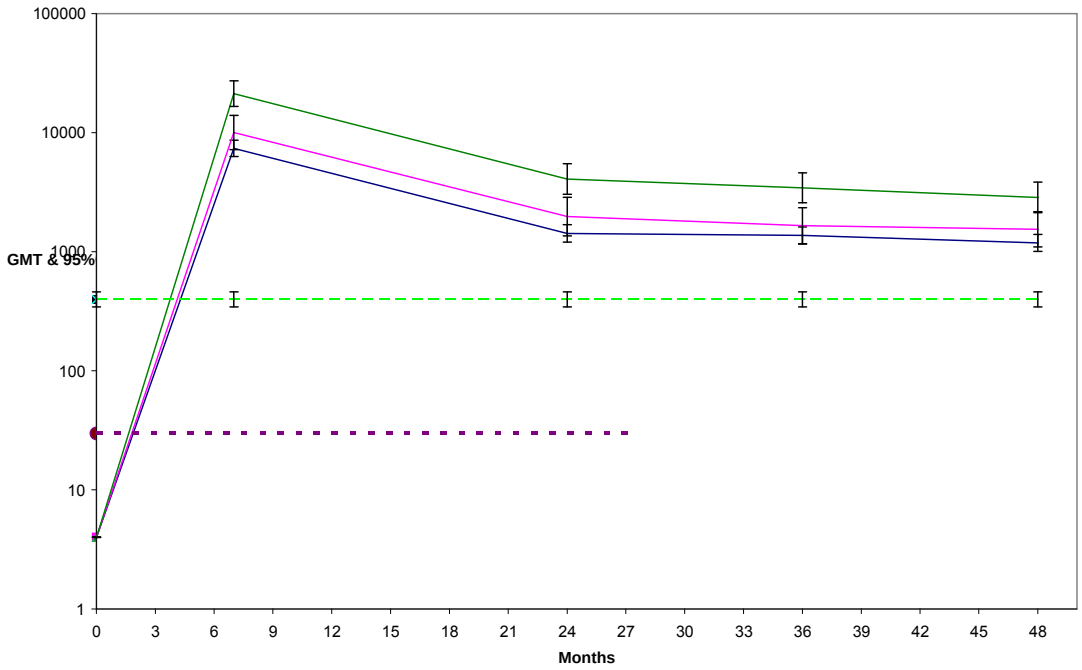
HPV-001 = HPV-001 study (ATP immunogenicity cohort), (Old_M) (15 ≤ Age ≤ 25)
N = number of subjects with available results
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Seroconversion rates and GMTs for HPV-18 IgG antibodies at Month 7 (Total Vaccinated Cohort)

Group	N	≥ 7 EU/mL				GMT (EU/mL)		
				95% CI			95% CI	
		n	%	LL	UL	value	LL	UL
HPV-001	325	325	100	98.9	100	3471.8	3161.9	3811.9
Pooled_lots	373	373	100	99.0	100	3369.8	3071.7	3696.7

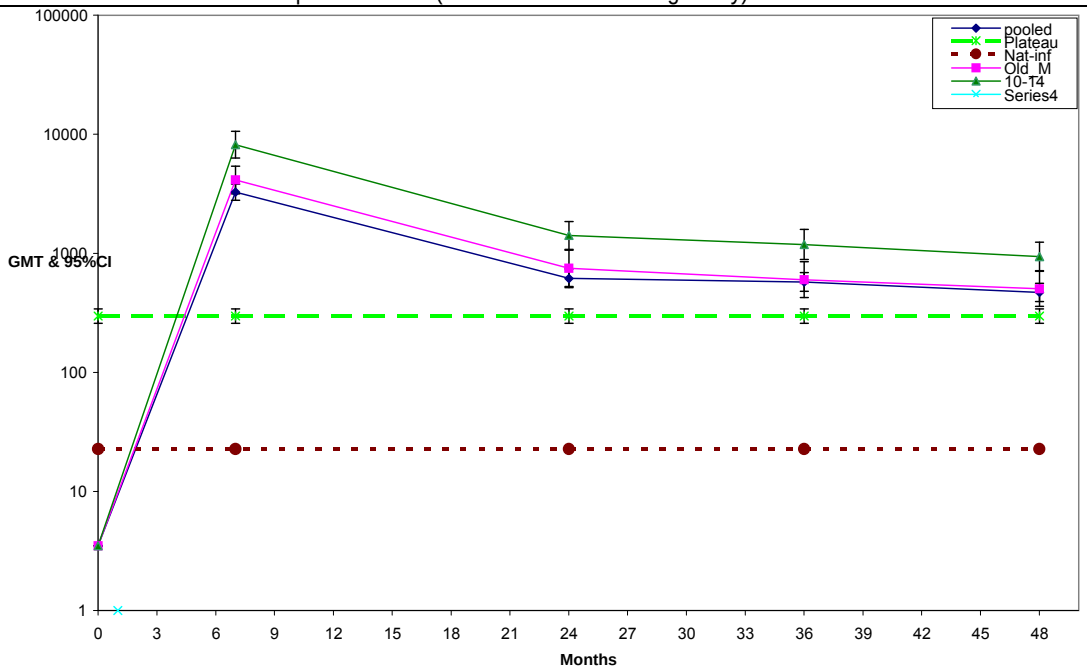
HPV-001 = HPV-001 study (ATP immunogenicity cohort), (Old_M) (15 ≤ Age ≤ 25)
N = number of subjects with available results
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Kinetics of Anti-HPV-16 antibodies up to Month 48 (ATP cohort for immunogenicity)



Pooled = pooled lots Group
Old_M= Old _ M Group
10-14 = [10-14] Group
Plateau = plateau phase from Study HPV-007 (corresponding to the time point Month 45 - 50 at Month 24 interim analysis, Total cohort, GMTs = 397.8 EL.U/mL)
Nat inf = subjects from study HPV-008 who are at baseline HPV-16 DNA negative and HPV-16 seropositive (i.e., who cleared a natural infection)

Secondary Outcome Variable (s):
Kinetics of Anti-HPV-18 antibodies up to Month 48 (ATP cohort for immunogenicity)



Pooled = pooled lots Group
Old_M= Old _ M Group
10-14 = [10-14] Group
Plateau = plateau phase from Study HPV-007 (corresponding to the time point Month 45 - 50 at Month 24 interim analysis, Total cohort, GMTs = 397.8 EL.U/mL)
Nat inf = subjects from study HPV-008 who are at baseline HPV-16 DNA negative and HPV-16 seropositive (i.e., who cleared a natural infection)

Secondary Outcome Variable (s):
Serum seropositivity rates and GMTs for HPV-16 and HPV-18 CVS* antibodies at Month 24 (Total Vaccinated cohort)

Antibody	Group	Timing	N	≥ LOQ (EU/mL)				GMT (EU/mL)		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
HPV-16 Secretion	Pooled_lots	PIII (M24)	55	47	85.5	73.3	93.5	85.4	57.9	125.8
	Old_M	PIII (M24)	13	9	69.2	38.6	90.9	107.5	47.5	242.8
	[10-14]	PIII (M24)	1	1	100	2.5	100	198.8	-	-
HPV-18 Secretion	Pooled_lots	PIII (M24)	55	40	72.7	59.0	83.9	45.9	31.1	67.6
	Old_M	PIII (M24)	13	9	69.2	38.6	90.9	31.9	15.8	64.4
	[10-14]	PIII (M24)	1	1	100	2.5	100	107.9	-	-

*CVS samples with < 80 erythrocytes/μL
LOQ = Limit of Quantification
N = number of subjects with available results
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PIII(M24) = Post Dose III (Month 24)

Secondary Outcome Variable (s):
Seropositivity rates and GMTs for anti-HPV-16 IgG antibodies for the subjects having CVS* samples results available (Total Vaccinated cohort)

Group	Timing	N	≥ 8 EU/ML				GMT (EU/ML)		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
Pooled_lots	PRE	53	7	13.2	5.5	25.3	5.4	4.2	6.9
	PIII(M7)	55	55	100	93.5	100	7735.5	5921.2	10105.6
	PIII (M24)	55	55	100	93.5	100	1592.8	1234.1	2055.7
Old_M	PRE	13	4	30.8	9.1	61.4	9.9	3.5	28.1
	PIII(M7)	13	13	100	75.3	100	5618.2	3014.4	10471.3
	PIII (M24)	13	13	100	75.3	100	1319.6	676.4	2574.6
[10-14]	PIII(M7)	1	1	100	2.5	100	11105.0	-	-

* CVS samples < 80 erythrocytes/μL
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination
PIII(M7) = Post Dose III (Month 7)
PIII(M24) = Post Dose III (Month 24)

Secondary Outcome Variable (s):
Seropositivity rates and GMTs for anti-HPV-18 IgG antibodies for the subjects having CVS* samples results available (Total Vaccinated cohort)

Group	Timing	N	≥ 7 EU/ML				GMT (EU/ML)		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
Pooled_lots	PRE	54	7	13.0	5.4	24.9	4.7	3.7	5.9
	PIII(M7)	55	55	100	93.5	100	3229.2	2547.9	4092.5
	PIII (M24)	55	55	100	93.5	100	650.6	503.4	840.9

Old_M	PRE	12	3	25.0	5.5	57.2	6.4	2.9	13.8
	PIII(M7)	13	13	100	75.3	100	2532.9	1589.8	4035.5
	PIII (M24)	13	13	100	75.3	100	464.8	259.9	831.2
[10-14]	PIII(M7)	1	1	100	2.5	100	4541.0	-	-

* CVS samples < 80 erythrocytes/μL
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination
PIII(M7) = Post Dose III (Month 7)
PIII(M24) = Post Dose III (Month 24)

Secondary Outcome Variable (s):
Serum seropositivity rates and GMTs for HPV-16 and HPV-18 CVS* antibodies at Month 36 (Total Vaccinated cohort)

Antibody	Group	Timing	N	≥ LOQ (EU/mL)				GMT (EU/mL)		
				n	%	95% CI		Value	95% CI	
						LL	UL		LL	UL
HPV-16 Secretion	Pooled_lots	PIII(M36)	78	68	87.2	77.7	93.7	68.2	54.6	85.2
	Old_M	PIII(M36)	27	23	85.2	66.3	95.8	62.1	40.8	94.7
	[10-14]	PIII(M36)	3	3	100	29.2	100	63.4	4.8	845.9
HPV-18 Secretion	Pooled_lots	PIII(M36)	78	56	71.8	60.5	81.4	38.9	31.2	48.6
	Old_M	PIII(M36)	27	20	74.1	53.7	88.9	29.6	19.8	44.2
	[10-14]	PIII(M36)	3	3	100	29.2	100	19.9	1.1	362.2

* CVS samples < 200 erythrocytes/μL
LOQ = Limit of Quantification
N = number of subjects with available results
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PIII(M36) = Post Dose III (Month 36)

Secondary Outcome Variable (s):
Seropositivity rates and GMTs of anti-HPV-16 and -18 IgG-antibodies present in CVS* at Month 48 (Total Vaccinated cohort)

				≥LOQ (EU/ML)				GMT (EU/mL)		
						95% CI			95% CI	
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL
HPV-16 Secretion	Pooled_lots	PIII(M48)	69	58	84.1	73.3	91.8	56.2	43.4	72.8
	Old_M	PIII(M48)	19	15	78.9	54.4	93.9	94.5	50.8	175.8
	[10-14]	PIII(M48)	4	4	100	39.8	100	129.2	12.8	1305.0
HPV-18 Secretion	Pooled_lots	PIII(M48)	66	46	69.7	57.1	80.4	33.9	24.7	46.5
	Old_M	PIII(M48)	19	14	73.7	48.8	90.9	48.8	26.4	90.0
	[10-14]	PIII(M48)	4	3	75.0	19.4	99.4	97.5	38.7	245.4

* CVS samples ≤ 200 erythrocytes/μL
LOQ = Limit of Quantification
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PIII(M48) = Post Dose III (Month 48)

Secondary Outcome Variable (s):
Seropositivity rates and GMTs for anti-HPV-16 IgG antibodies for the subjects having CVS* samples results available (Total Vaccinated cohort)

Group	Timing	N	≥ 8 EU/ML				GMT (EU/ML)		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
Pooled_lots	PRE	77	21	27.3	17.7	38.6	7.4	5.7	9.6

	PIII(M7)	77	77	100	95.3	100	6294.9	5005.8	7916.1
	PIII(M18)	1	1	100	2.5	100	291.0	-	-
	PIII(M24)	74	74	100	95.1	100	1403.1	1126.9	1747.0
	PIII(M36)	78	78	100	95.4	100	1291.8	1030.9	1618.7
	PIII(M48)	69	69	100	94.8	100	1047.3	854.2	1284.0
Old_M	PRE	27	6	22.2	8.6	42.3	8.3	4.6	14.9
	PIII(M7)	27	27	100	87.2	100	7693.9	5185.7	11415.3
	PIII(M24)	24	24	100	85.8	100	1490.5	1016.1	2186.5
	PIII(M36)	27	27	100	87.2	100	1435.0	993.0	2073.8
	PIII(M48)	19	19	100	82.4	100	1950.5	1095.1	3474.1
[10-14]	PRE	3	0	0.0	0.0	70.8	4.0	4.0	4.0
	PIII(M7)	3	3	100	29.2	100	25143.3	12120.8	52156.9
	PIII(M24)	3	3	100	29.2	100	5399.5	367.9	79243.9
	PIII(M36)	3	3	100	29.2	100	3733.3	383.1	36384.7
	PIII(M48)	4	4	100	39.8	100	3332.7	1087.6	10212.5

* CVS samples < 200 erythrocytes/μL
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination
PIII(M7) = Post Dose III (Month 7)
PIII(M24) = Post Dose III (Month 24)
PIII(M36) = Post Dose III (Month 36)
PIII(M48) = Post Dose III (Month 48)

Secondary Outcome Variable (s):
Seropositivity rates and GMTs for anti-HPV-18 IgG antibodies for the subjects having CVS* samples results available (Total Vaccinated cohort)

Group	Timing	N	≥ 7 EU/ML				GMT (EU/ML)		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
Pooled_lots	PRE	78	16	20.5	12.2	31.2	6.1	4.6	8.1
	PIII(M7)	77	77	100	95.3	100	2880.5	2297.2	3612.0
	PIII(M18)	1	1	100	2.5	100	604.0	-	-
	PIII(M24)	74	74	100	95.1	100	584.5	461.1	741.0
	PIII(M36)	78	78	100	95.4	100	555.4	439.3	702.1
	PIII(M48)	66	66	100	94.6	100	478.4	376.8	607.3
Old_M	PRE	26	6	23.1	9.0	43.6	6.3	3.9	10.3
	PIII(M7)	27	27	100	87.2	100	3788.5	2802.8	5120.8
	PIII(M24)	24	24	100	85.8	100	648.6	467.7	899.6
	PIII(M36)	27	27	100	87.2	100	542.1	392.8	748.0
	PIII(M48)	19	19	100	82.4	100	805.4	491.2	1320.5
[10-14]	PRE	2	0	0.0	0.0	84.2	3.5	3.5	3.5
	PIII(M7)	3	3	100	29.2	100	6047.1	1331.6	27461.9
	PIII(M24)	3	3	100	29.2	100	1814.6	240.3	13702.9
	PIII(M36)	3	3	100	29.2	100	1163.6	88.8	15244.0
	PIII(M48)	4	4	100	39.8	100	1048.9	250.5	4392.8

* CVS samples < 200 erythrocytes/μL
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination
PIII(M7) = Post Dose III (Month 7)
PIII(M24) = Post Dose III (Month 24)
PIII(M36) = Post Dose III (Month 36)
PIII(M48) = Post Dose III (Month 48)

Secondary Outcome Variable (s):

Incidence of solicited local symptoms reported during the 7-day (Day 0-6) post-vaccination period following each dose and overall (Total Vaccinated Cohort)																
Symptom	Intensity	Lot 1 Group					Lot 2 Group					Lot 3 Group				
		N	n	%	95% CI		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL				LL	UL
Dose 1																
Pain	Any	154	142	92.2	86.8	95.9	153	138	90.2	84.3	94.4	145	128	88.3	81.9	93.0
	Grade 3	154	7	4.5	1.8	9.1	153	8	5.2	2.3	10.0	145	6	4.1	1.5	8.8
Redness	Any	154	47	30.5	23.4	38.4	153	48	31.4	24.1	39.4	145	53	36.6	28.7	44.9
	> 50 mm	154	0	0.0	0.0	2.4	153	2	1.3	0.2	4.6	145	0	0.0	0.0	2.5
Swelling	Any	154	37	24.0	17.5	31.6	153	43	28.1	21.1	35.9	145	39	26.9	19.9	34.9
	> 50 mm	154	1	0.6	0.0	3.6	153	3	2.0	0.4	5.6	145	3	2.1	0.4	5.9
Dose 2																
Pain	Any	151	128	84.8	78.0	90.1	150	123	82.0	74.9	87.8	145	119	82.1	74.8	87.9
	Grade 3	151	7	4.6	1.9	9.3	150	8	5.3	2.3	10.2	145	4	2.8	0.8	6.9
Redness	Any	151	65	43.0	35.0	51.3	150	59	39.3	31.5	47.6	145	68	46.9	38.6	55.4
	> 50 mm	151	1	0.7	0.0	3.6	150	1	0.7	0.0	3.7	145	2	1.4	0.2	4.9
Swelling	Any	151	57	37.7	30.0	46.0	150	52	34.7	27.1	42.9	145	52	35.9	28.1	44.2
	> 50 mm	151	5	3.3	1.1	7.6	150	2	1.3	0.2	4.7	145	3	2.1	0.4	5.9
Dose 3																
Pain	Any	149	129	86.6	80.0	91.6	149	121	81.2	74.0	87.1	145	119	82.1	74.8	87.9
	Grade 3	149	9	6.0	2.8	11.2	149	10	6.7	3.3	12.0	145	10	6.9	3.4	12.3
Redness	Any	149	71	47.7	39.4	56.0	149	60	40.3	32.3	48.6	145	59	40.7	32.6	49.2
	> 50 mm	149	5	3.4	1.1	7.7	149	3	2.0	0.4	5.8	145	3	2.1	0.4	5.9
Swelling	Any	149	60	40.3	32.3	48.6	149	58	38.9	31.1	47.2	145	50	34.5	26.8	42.8
	> 50 mm	149	1	0.7	0.0	3.7	149	1	0.7	0.0	3.7	145	3	2.1	0.4	5.9
Across Doses																
Pain	Any	154	148	96.1	91.7	98.6	153	148	96.7	92.5	98.9	145	137	94.5	89.4	97.6
	Grade 3	154	17	11.0	6.6	17.1	153	19	12.4	7.6	18.7	145	18	12.4	7.5	18.9
Redness	Any	154	87	56.5	48.3	64.5	153	86	56.2	48.0	64.2	145	88	60.7	52.2	68.7
	> 50 mm	154	5	3.2	1.1	7.4	153	4	2.6	0.7	6.6	145	3	2.1	0.4	5.9
Swelling	Any	154	75	48.7	40.6	56.9	153	78	51.0	42.8	59.1	145	71	49.0	40.6	57.4
	> 50 mm	154	6	3.9	1.4	8.3	153	5	3.3	1.1	7.5	145	5	3.4	1.1	7.9
		Pooled_lots Group					Old_M Group					[10-14] Group				
Dose 1																
Pain	Any	452	408	90.3	87.2	92.8	153	138	90.2	84.3	94.4	155	136	87.7	81.5	92.5
	Grade 3	452	21	4.6	2.9	7.0	153	13	8.5	4.6	14.1	155	3	1.9	0.4	5.6
Redness	Any	452	148	32.7	28.4	37.3	153	50	32.7	25.3	40.7	155	51	32.9	25.6	40.9
	> 50 mm	452	2	0.4	0.1	1.6	153	0	0.0	0.0	2.4	155	1	0.6	0.0	3.5
Swelling	Any	452	119	26.3	22.3	30.6	153	38	24.8	18.2	32.5	155	44	28.4	21.4	36.2
	> 50 mm	452	7	1.5	0.6	3.2	153	2	1.3	0.2	4.6	155	2	1.3	0.2	4.6
Dose 2																
Pain	Any	446	370	83.0	79.1	86.3	150	126	84.0	77.1	89.5	154	125	81.2	74.1	87.0
	Grade 3	446	19	4.3	2.6	6.6	150	8	5.3	2.3	10.2	154	6	3.9	1.4	8.3
Redness	Any	446	192	43.0	38.4	47.8	150	62	41.3	33.4	49.7	154	59	38.3	30.6	46.5
	> 50 mm	446	4	0.9	0.2	2.3	150	2	1.3	0.2	4.7	154	2	1.3	0.2	4.6
Swelling	Any	446	161	36.1	31.6	40.7	150	41	27.3	20.4	35.2	154	53	34.4	27.0	42.5
	> 50 mm	446	10	2.2	1.1	4.1	150	2	1.3	0.2	4.7	154	2	1.3	0.2	4.6
Dose 3																
Pain	Any	443	369	83.3	79.5	86.6	147	128	87.1	80.6	92.0	154	126	81.8	74.8	87.6
	Grade 3	443	29	6.5	4.4	9.3	147	10	6.8	3.3	12.2	154	8	5.2	2.3	10.0
Redness	Any	443	190	42.9	38.2	47.6	147	62	42.2	34.1	50.6	154	55	35.7	28.2	43.8
	> 50 mm	443	11	2.5	1.2	4.4	147	1	0.7	0.0	3.7	154	1	0.6	0.0	3.6
Swelling	Any	443	168	37.9	33.4	42.6	147	50	34.0	26.4	42.3	154	58	37.7	30.0	45.8
	> 50 mm	443	5	1.1	0.4	2.6	147	3	2.0	0.4	5.8	154	2	1.3	0.2	4.6

Across Doses																
Pain	Any	452	433	95.8	93.5	97.5	153	148	96.7	92.5	98.9	155	147	94.8	90.1	97.7
	Grade 3	452	54	11.9	9.1	15.3	153	23	15.0	9.8	21.7	155	12	7.7	4.1	13.1
Redness	Any	452	261	57.7	53.0	62.3	153	88	57.5	49.3	65.5	155	91	58.7	50.5	66.5
	> 50 mm	452	12	2.7	1.4	4.6	153	3	2.0	0.4	5.6	155	3	1.9	0.4	5.6
Swelling	Any	452	224	49.6	44.9	54.3	153	72	47.1	38.9	55.3	155	83	53.5	45.4	61.6
	> 50 mm	452	16	3.5	2.0	5.7	153	5	3.3	1.1	7.5	155	4	2.6	0.7	6.5

N = number of subjects with a documented dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = lower limit, UL = upper limit
Any= any solicited local symptom irrespective 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 (Day 0-6) post-vaccination period following each dose and overall (Total Vaccinated Cohort)

Symptom	Intensity/ relation-ship	Lot 1 Group					Lot 2 Group					Lot 3 Group				
		N	n	%	95% CI		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL				LL	UL
Dose 1																
Arthralgia	Any	155	15	9.7	5.5	15.5	153	12	7.8	4.1	13.3	145	19	13.1	8.1	19.7
	Grade 3	155	1	0.6	0.0	3.5	153	1	0.7	0.0	3.6	145	0	0.0	0.0	2.5
	Related	155	11	7.1	3.6	12.3	153	10	6.5	3.2	11.7	145	15	10.3	5.9	16.5
Fatigue	Any	155	55	35.5	28.0	43.6	153	47	30.7	23.5	38.7	145	53	36.6	28.7	44.9
	Grade 3	155	1	0.6	0.0	3.5	153	2	1.3	0.2	4.6	145	2	1.4	0.2	4.9
	Related	155	35	22.6	16.3	30.0	153	26	17.0	11.4	23.9	145	34	23.4	16.8	31.2
Fever (axillary)	≥ 37.5 °C	155	4	2.6	0.7	6.5	153	5	3.3	1.1	7.5	145	5	3.4	1.1	7.9
	> 39.0 °C	155	0	0.0	0.0	2.4	153	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	155	1	0.6	0.0	3.5	153	3	2.0	0.4	5.6	145	3	2.1	0.4	5.9
Gastro-intestinal	Any	155	24	15.5	10.2	22.2	153	27	17.6	12.0	24.6	145	36	24.8	18.0	32.7
	Grade 3	155	0	0.0	0.0	2.4	153	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	155	12	7.7	4.1	13.1	153	11	7.2	3.6	12.5	145	16	11.0	6.4	17.3
Headache	Any	155	54	34.8	27.4	42.9	153	50	32.7	25.3	40.7	145	47	32.4	24.9	40.7
	Grade 3	155	2	1.3	0.2	4.6	153	5	3.3	1.1	7.5	145	1	0.7	0.0	3.8
	Related	155	27	17.4	11.8	24.3	153	23	15.0	9.8	21.7	145	22	15.2	9.8	22.1
Myalgia	Any	155	52	33.5	26.2	41.6	153	55	35.9	28.4	44.1	145	51	35.2	27.4	43.5
	Grade 3	155	2	1.3	0.2	4.6	153	2	1.3	0.2	4.6	145	1	0.7	0.0	3.8
	Related	155	46	29.7	22.6	37.5	153	46	30.1	22.9	38.0	145	42	29.0	21.7	37.1
Rash	Any	155	7	4.5	1.8	9.1	153	7	4.6	1.9	9.2	145	9	6.2	2.9	11.5
	Grade 3	155	1	0.6	0.0	3.5	153	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	155	6	3.9	1.4	8.2	153	3	2.0	0.4	5.6	145	3	2.1	0.4	5.9
Urticaria	Any	155	1	0.6	0.0	3.5	153	1	0.7	0.0	3.6	145	3	2.1	0.4	5.9
	Grade 3	155	0	0.0	0.0	2.4	153	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	155	1	0.6	0.0	3.5	153	1	0.7	0.0	3.6	145	2	1.4	0.2	4.9
Dose 2																
Arthralgia	Any	151	16	10.6	6.2	16.6	150	10	6.7	3.2	11.9	145	18	12.4	7.5	18.9
	Grade 3	151	1	0.7	0.0	3.6	150	0	0.0	0.0	2.4	145	1	0.7	0.0	3.8
	Related	151	14	9.3	5.2	15.1	150	8	5.3	2.3	10.2	145	17	11.7	7.0	18.1
Fatigue	Any	151	50	33.1	25.7	41.2	150	31	20.7	14.5	28.0	145	36	24.8	18.0	32.7
	Grade 3	151	0	0.0	0.0	2.4	150	0	0.0	0.0	2.4	145	1	0.7	0.0	3.8
	Related	151	35	23.2	16.7	30.7	150	21	14.0	8.9	20.6	145	26	17.9	12.1	25.2
Fever (axillary)	≥ 37.5 °C	151	8	5.3	2.3	10.2	150	3	2.0	0.4	5.7	145	6	4.1	1.5	8.8
	> 39.0 °C	151	0	0.0	0.0	2.4	150	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	151	5	3.3	1.1	7.6	150	3	2.0	0.4	5.7	145	4	2.8	0.8	6.9
Gastro-	Any	151	12	7.9	4.2	13.5	150	16	10.7	6.2	16.7	145	18	12.4	7.5	18.9

intestinal	Grade 3	151	1	0.7	0.0	3.6	150	0	0.0	0.0	2.4	145	1	0.7	0.0	3.8
	Related	151	5	3.3	1.1	7.6	150	5	3.3	1.1	7.6	145	12	8.3	4.3	14.0
Headache	Any	151	57	37.7	30.0	46.0	150	33	22.0	15.7	29.5	145	41	28.3	21.1	36.3
	Grade 3	151	0	0.0	0.0	2.4	150	0	0.0	0.0	2.4	145	3	2.1	0.4	5.9
	Related	151	31	20.5	14.4	27.9	150	19	12.7	7.8	19.1	145	25	17.2	11.5	24.4
Myalgia	Any	151	40	26.5	19.6	34.3	150	40	26.7	19.8	34.5	145	43	29.7	22.4	37.8
	Grade 3	151	2	1.3	0.2	4.7	150	2	1.3	0.2	4.7	145	1	0.7	0.0	3.8
	Related	151	32	21.2	15.0	28.6	150	38	25.3	18.6	33.1	145	38	26.2	19.3	34.2
Rash	Any	151	3	2.0	0.4	5.7	150	6	4.0	1.5	8.5	145	9	6.2	2.9	11.5
	Grade 3	151	0	0.0	0.0	2.4	150	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	151	3	2.0	0.4	5.7	150	5	3.3	1.1	7.6	145	7	4.8	2.0	9.7
Urticaria	Any	151	3	2.0	0.4	5.7	150	5	3.3	1.1	7.6	145	3	2.1	0.4	5.9
	Grade 3	151	0	0.0	0.0	2.4	150	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	151	3	2.0	0.4	5.7	150	4	2.7	0.7	6.7	145	3	2.1	0.4	5.9
Dose 3																
Arthralgia	Any	149	13	8.7	4.7	14.5	149	9	6.0	2.8	11.2	145	13	9.0	4.9	14.8
	Grade 3	149	0	0.0	0.0	2.4	149	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	149	11	7.4	3.7	12.8	149	8	5.4	2.3	10.3	145	9	6.2	2.9	11.5
Fatigue	Any	149	39	26.2	19.3	34.0	149	46	30.9	23.6	39.0	145	42	29.0	21.7	37.1
	Grade 3	149	1	0.7	0.0	3.7	149	1	0.7	0.0	3.7	145	3	2.1	0.4	5.9
	Related	149	27	18.1	12.3	25.3	149	32	21.5	15.2	28.9	145	30	20.7	14.4	28.2
Fever (axillary)	≥ 37.5 °C	149	5	3.4	1.1	7.7	149	7	4.7	1.9	9.4	145	3	2.1	0.4	5.9
	> 39.0 °C	149	0	0.0	0.0	2.4	149	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	149	2	1.3	0.2	4.8	149	5	3.4	1.1	7.7	145	3	2.1	0.4	5.9
Gastro-intestinal	Any	149	18	12.1	7.3	18.4	149	14	9.4	5.2	15.3	145	22	15.2	9.8	22.1
	Grade 3	149	1	0.7	0.0	3.7	149	0	0.0	0.0	2.4	145	2	1.4	0.2	4.9
	Related	149	10	6.7	3.3	12.0	149	7	4.7	1.9	9.4	145	12	8.3	4.3	14.0
Headache	Any	149	43	28.9	21.7	36.8	149	40	26.8	19.9	34.7	145	37	25.5	18.6	33.4
	Grade 3	149	1	0.7	0.0	3.7	149	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	149	24	16.1	10.6	23.0	149	21	14.1	8.9	20.7	145	23	15.9	10.3	22.8
Myalgia	Any	149	40	26.8	19.9	34.7	149	40	26.8	19.9	34.7	145	42	29.0	21.7	37.1
	Grade 3	149	2	1.3	0.2	4.8	149	3	2.0	0.4	5.8	145	1	0.7	0.0	3.8
	Related	149	30	20.1	14.0	27.5	149	36	24.2	17.5	31.8	145	35	24.1	17.4	31.9
Rash	Any	149	3	2.0	0.4	5.8	149	4	2.7	0.7	6.7	145	2	1.4	0.2	4.9
	Grade 3	149	0	0.0	0.0	2.4	149	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	149	1	0.7	0.0	3.7	149	3	2.0	0.4	5.8	145	1	0.7	0.0	3.8
Urticaria	Any	149	2	1.3	0.2	4.8	149	1	0.7	0.0	3.7	145	3	2.1	0.4	5.9
	Grade 3	149	0	0.0	0.0	2.4	149	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	149	1	0.7	0.0	3.7	149	1	0.7	0.0	3.7	145	2	1.4	0.2	4.9
Across Doses																
Arthralgia	Any	155	30	19.4	13.5	26.5	153	21	13.7	8.7	20.2	145	30	20.7	14.4	28.2
	Grade 3	155	2	1.3	0.2	4.6	153	1	0.7	0.0	3.6	145	1	0.7	0.0	3.8
	Related	155	24	15.5	10.2	22.2	153	17	11.1	6.6	17.2	145	24	16.6	10.9	23.6
Fatigue	Any	155	76	49.0	40.9	57.2	153	67	43.8	35.8	52.0	145	76	52.4	44.0	60.8
	Grade 3	155	2	1.3	0.2	4.6	153	2	1.3	0.2	4.6	145	6	4.1	1.5	8.8
	Related	155	58	37.4	29.8	45.5	153	52	34.0	26.5	42.1	145	59	40.7	32.6	49.2
Fever (axillary)	≥ 37.5 °C	155	16	10.3	6.0	16.2	153	13	8.5	4.6	14.1	145	14	9.7	5.4	15.7
	> 39.0 °C	155	0	0.0	0.0	2.4	153	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	155	8	5.2	2.3	9.9	153	9	5.9	2.7	10.9	145	10	6.9	3.4	12.3
Gastro-intestinal	Any	155	37	23.9	17.4	31.4	153	45	29.4	22.3	37.3	145	54	37.2	29.4	45.7
	Grade 3	155	2	1.3	0.2	4.6	153	0	0.0	0.0	2.4	145	3	2.1	0.4	5.9
	Related	155	21	13.5	8.6	20.0	153	21	13.7	8.7	20.2	145	29	20.0	13.8	27.4
Headache	Any	155	88	56.8	48.6	64.7	153	75	49.0	40.9	57.2	145	79	54.5	46.0	62.8
	Grade 3	155	3	1.9	0.4	5.6	153	5	3.3	1.1	7.5	145	4	2.8	0.8	6.9
	Related	155	58	37.4	29.8	45.5	153	45	29.4	22.3	37.3	145	52	35.9	28.1	44.2

Myalgia	Any	155	68	43.9	35.9	52.1	153	73	47.7	39.6	55.9	145	61	42.1	33.9	50.5
	Grade 3	155	4	2.6	0.7	6.5	153	5	3.3	1.1	7.5	145	3	2.1	0.4	5.9
	Related	155	60	38.7	31.0	46.9	153	66	43.1	35.2	51.4	145	54	37.2	29.4	45.7
Rash	Any	155	13	8.4	4.5	13.9	153	13	8.5	4.6	14.1	145	18	12.4	7.5	18.9
	Grade 3	155	1	0.6	0.0	3.5	153	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	155	10	6.5	3.1	11.5	153	9	5.9	2.7	10.9	145	11	7.6	3.8	13.2
Urticaria	Any	155	4	2.6	0.7	6.5	153	6	3.9	1.5	8.3	145	8	5.5	2.4	10.6
	Grade 3	155	0	0.0	0.0	2.4	153	0	0.0	0.0	2.4	145	0	0.0	0.0	2.5
	Related	155	3	1.9	0.4	5.6	153	5	3.3	1.1	7.5	145	6	4.1	1.5	8.8
		Pooled_lots Group					Old_M Group					[10-14] Group				
Dose 1																
Arthralgia	Any	453	46	10.2	7.5	13.3	153	16	10.5	6.1	16.4	155	15	9.7	5.5	15.5
	Grade 3	453	2	0.4	0.1	1.6	153	1	0.7	0.0	3.6	155	0	0.0	0.0	2.4
	Related	453	36	7.9	5.6	10.8	153	9	5.9	2.7	10.9	155	10	6.5	3.1	11.5
Fatigue	Any	453	155	34.2	29.9	38.8	153	54	35.3	27.7	43.4	155	45	29.0	22.0	36.9
	Grade 3	453	5	1.1	0.4	2.6	153	6	3.9	1.5	8.3	155	1	0.6	0.0	3.5
	Related	453	95	21.0	17.3	25.0	153	30	19.6	13.6	26.8	155	21	13.5	8.6	20.0
Fever (axillary)	≥ 37.5 °C	453	14	3.1	1.7	5.1	153	6	3.9	1.5	8.3	155	4	2.6	0.7	6.5
	> 39.0 °C	453	0	0.0	0.0	0.8	153	0	0.0	0.0	2.4	155	0	0.0	0.0	2.4
	Related	453	7	1.5	0.6	3.2	153	4	2.6	0.7	6.6	155	3	1.9	0.4	5.6
Gastro-intestinal	Any	453	87	19.2	15.7	23.1	153	29	19.0	13.1	26.1	155	22	14.2	9.1	20.7
	Grade 3	453	0	0.0	0.0	0.8	153	1	0.7	0.0	3.6	155	0	0.0	0.0	2.4
	Related	453	39	8.6	6.2	11.6	153	10	6.5	3.2	11.7	155	5	3.2	1.1	7.4
Headache	Any	453	151	33.3	29.0	37.9	153	60	39.2	31.4	47.4	155	54	34.8	27.4	42.9
	Grade 3	453	8	1.8	0.8	3.4	153	1	0.7	0.0	3.6	155	0	0.0	0.0	2.4
	Related	453	72	15.9	12.6	19.6	153	28	18.3	12.5	25.4	155	17	11.0	6.5	17.0
Myalgia	Any	453	158	34.9	30.5	39.5	153	60	39.2	31.4	47.4	155	46	29.7	22.6	37.5
	Grade 3	453	5	1.1	0.4	2.6	153	3	2.0	0.4	5.6	155	1	0.6	0.0	3.5
	Related	453	134	29.6	25.4	34.0	153	49	32.0	24.7	40.0	155	30	19.4	13.5	26.5
Rash	Any	453	23	5.1	3.2	7.5	153	6	3.9	1.5	8.3	155	9	5.8	2.7	10.7
	Grade 3	453	1	0.2	0.0	1.2	153	0	0.0	0.0	2.4	155	0	0.0	0.0	2.4
	Related	453	12	2.6	1.4	4.6	153	4	2.6	0.7	6.6	155	4	2.6	0.7	6.5
Urticaria	Any	453	5	1.1	0.4	2.6	153	3	2.0	0.4	5.6	155	1	0.6	0.0	3.5
	Grade 3	453	0	0.0	0.0	0.8	153	0	0.0	0.0	2.4	155	0	0.0	0.0	2.4
	Related	453	4	0.9	0.2	2.2	153	2	1.3	0.2	4.6	155	1	0.6	0.0	3.5
Dose 2																
Arthralgia	Any	446	44	9.9	7.3	13.0	150	19	12.7	7.8	19.1	154	14	9.1	5.1	14.8
	Grade 3	446	2	0.4	0.1	1.6	150	0	0.0	0.0	2.4	154	0	0.0	0.0	2.4
	Related	446	39	8.7	6.3	11.8	150	15	10.0	5.7	16.0	154	9	5.8	2.7	10.8
Fatigue	Any	446	117	26.2	22.2	30.6	150	34	22.7	16.2	30.2	154	45	29.2	22.2	37.1
	Grade 3	446	1	0.2	0.0	1.2	150	3	2.0	0.4	5.7	154	4	2.6	0.7	6.5
	Related	446	82	18.4	14.9	22.3	150	19	12.7	7.8	19.1	154	25	16.2	10.8	23.0
Fever (axillary)	≥ 37.5 °C	446	17	3.8	2.2	6.0	150	6	4.0	1.5	8.5	154	9	5.8	2.7	10.8
	> 39.0 °C	446	0	0.0	0.0	0.8	150	0	0.0	0.0	2.4	154	2	1.3	0.2	4.6
	Related	446	12	2.7	1.4	4.7	150	3	2.0	0.4	5.7	154	3	1.9	0.4	5.6
Gastro-intestinal	Any	446	46	10.3	7.7	13.5	150	18	12.0	7.3	18.3	154	13	8.4	4.6	14.0
	Grade 3	446	2	0.4	0.1	1.6	150	0	0.0	0.0	2.4	154	3	1.9	0.4	5.6
	Related	446	22	4.9	3.1	7.4	150	6	4.0	1.5	8.5	154	6	3.9	1.4	8.3
Headache	Any	446	131	29.4	25.2	33.8	150	38	25.3	18.6	33.1	154	34	22.1	15.8	29.5
	Grade 3	446	3	0.7	0.1	2.0	150	5	3.3	1.1	7.6	154	1	0.6	0.0	3.6
	Related	446	75	16.8	13.5	20.6	150	20	13.3	8.3	19.8	154	13	8.4	4.6	14.0
Myalgia	Any	446	123	27.6	23.5	32.0	150	40	26.7	19.8	34.5	154	47	30.5	23.4	38.4
	Grade 3	446	5	1.1	0.4	2.6	150	0	0.0	0.0	2.4	154	2	1.3	0.2	4.6
	Related	446	108	24.2	20.3	28.5	150	37	24.7	18.0	32.4	154	33	21.4	15.2	28.8
Rash	Any	446	18	4.0	2.4	6.3	150	4	2.7	0.7	6.7	154	8	5.2	2.3	10.0

	Grade 3	446	0	0.0	0.0	0.8	150	0	0.0	0.0	2.4	154	0	0.0	0.0	2.4
	Related	446	15	3.4	1.9	5.5	150	3	2.0	0.4	5.7	154	7	4.5	1.8	9.1
Urticaria	Any	446	11	2.5	1.2	4.4	150	1	0.7	0.0	3.7	154	3	1.9	0.4	5.6
	Grade 3	446	0	0.0	0.0	0.8	150	0	0.0	0.0	2.4	154	0	0.0	0.0	2.4
	Related	446	10	2.2	1.1	4.1	150	0	0.0	0.0	2.4	154	3	1.9	0.4	5.6
Dose 3																
Arthralgia	Any	443	35	7.9	5.6	10.8	147	15	10.2	5.8	16.3	154	16	10.4	6.1	16.3
	Grade 3	443	0	0.0	0.0	0.8	147	0	0.0	0.0	2.5	154	1	0.6	0.0	3.6
	Related	443	28	6.3	4.2	9.0	147	12	8.2	4.3	13.8	154	13	8.4	4.6	14.0
Fatigue	Any	443	127	28.7	24.5	33.1	147	45	30.6	23.3	38.7	154	47	30.5	23.4	38.4
	Grade 3	443	5	1.1	0.4	2.6	147	2	1.4	0.2	4.8	154	2	1.3	0.2	4.6
	Related	443	89	20.1	16.5	24.1	147	30	20.4	14.2	27.8	154	34	22.1	15.8	29.5
Fever (axillary)	≥ 37.5 °C	443	15	3.4	1.9	5.5	147	2	1.4	0.2	4.8	154	5	3.2	1.1	7.4
	> 39.0 °C	443	0	0.0	0.0	0.8	147	0	0.0	0.0	2.5	154	0	0.0	0.0	2.4
	Related	443	10	2.3	1.1	4.1	147	1	0.7	0.0	3.7	154	3	1.9	0.4	5.6
Gastro-intestinal	Any	443	54	12.2	9.3	15.6	147	16	10.9	6.4	17.1	154	20	13.0	8.1	19.3
	Grade 3	443	3	0.7	0.1	2.0	147	0	0.0	0.0	2.5	154	4	2.6	0.7	6.5
	Related	443	29	6.5	4.4	9.3	147	6	4.1	1.5	8.7	154	13	8.4	4.6	14.0
Headache	Any	443	120	27.1	23.0	31.5	147	34	23.1	16.6	30.8	154	38	24.7	18.1	32.3
	Grade 3	443	1	0.2	0.0	1.3	147	4	2.7	0.7	6.8	154	4	2.6	0.7	6.5
	Related	443	68	15.3	12.1	19.0	147	22	15.0	9.6	21.8	154	23	14.9	9.7	21.6
Myalgia	Any	443	122	27.5	23.4	32.0	147	36	24.5	17.8	32.3	154	47	30.5	23.4	38.4
	Grade 3	443	6	1.4	0.5	2.9	147	4	2.7	0.7	6.8	154	2	1.3	0.2	4.6
	Related	443	101	22.8	19.0	27.0	147	33	22.4	16.0	30.1	154	40	26.0	19.2	33.6
Rash	Any	443	9	2.0	0.9	3.8	147	8	5.4	2.4	10.4	154	7	4.5	1.8	9.1
	Grade 3	443	0	0.0	0.0	0.8	147	1	0.7	0.0	3.7	154	2	1.3	0.2	4.6
	Related	443	5	1.1	0.4	2.6	147	4	2.7	0.7	6.8	154	4	2.6	0.7	6.5
Urticaria	Any	443	6	1.4	0.5	2.9	147	0	0.0	0.0	2.5	154	1	0.6	0.0	3.6
	Grade 3	443	0	0.0	0.0	0.8	147	0	0.0	0.0	2.5	154	0	0.0	0.0	2.4
	Related	443	4	0.9	0.2	2.3	147	0	0.0	0.0	2.5	154	1	0.6	0.0	3.6
Across Doses																
Arthralgia	Any	453	81	17.9	14.5	21.7	153	29	19.0	13.1	26.1	155	31	20.0	14.0	27.2
	Grade 3	453	4	0.9	0.2	2.2	153	1	0.7	0.0	3.6	155	1	0.6	0.0	3.5
	Related	453	65	14.3	11.3	17.9	153	23	15.0	9.8	21.7	155	25	16.1	10.7	22.9
Fatigue	Any	453	219	48.3	43.7	53.1	153	79	51.6	43.4	59.8	155	77	49.7	41.6	57.8
	Grade 3	453	10	2.2	1.1	4.0	153	9	5.9	2.7	10.9	155	6	3.9	1.4	8.2
	Related	453	169	37.3	32.8	41.9	153	58	37.9	30.2	46.1	155	52	33.5	26.2	41.6
Fever (axillary)	≥ 37.5 °C	453	43	9.5	7.0	12.6	153	12	7.8	4.1	13.3	155	17	11.0	6.5	17.0
	> 39.0 °C	453	0	0.0	0.0	0.8	153	0	0.0	0.0	2.4	155	2	1.3	0.2	4.6
	Related	453	27	6.0	4.0	8.6	153	7	4.6	1.9	9.2	155	8	5.2	2.3	9.9
Gastro-intestinal	Any	453	136	30.0	25.8	34.5	153	43	28.1	21.1	35.9	155	36	23.2	16.8	30.7
	Grade 3	453	5	1.1	0.4	2.6	153	1	0.7	0.0	3.6	155	7	4.5	1.8	9.1
	Related	453	71	15.7	12.4	19.4	153	16	10.5	6.1	16.4	155	22	14.2	9.1	20.7
Headache	Any	453	242	53.4	48.7	58.1	153	80	52.3	44.1	60.4	155	77	49.7	41.6	57.8
	Grade 3	453	12	2.6	1.4	4.6	153	8	5.2	2.3	10.0	155	5	3.2	1.1	7.4
	Related	453	155	34.2	29.9	38.8	153	49	32.0	24.7	40.0	155	43	27.7	20.9	35.5
Myalgia	Any	453	202	44.6	40.0	49.3	153	79	51.6	43.4	59.8	155	72	46.5	38.4	54.6
	Grade 3	453	12	2.6	1.4	4.6	153	6	3.9	1.5	8.3	155	2	1.3	0.2	4.6
	Related	453	180	39.7	35.2	44.4	153	73	47.7	39.6	55.9	155	59	38.1	30.4	46.2
Rash	Any	453	44	9.7	7.1	12.8	153	16	10.5	6.1	16.4	155	16	10.3	6.0	16.2
	Grade 3	453	1	0.2	0.0	1.2	153	1	0.7	0.0	3.6	155	2	1.3	0.2	4.6
	Related	453	30	6.6	4.5	9.3	153	9	5.9	2.7	10.9	155	9	5.8	2.7	10.7
Urticaria	Any	453	18	4.0	2.4	6.2	153	4	2.6	0.7	6.6	155	4	2.6	0.7	6.5
	Grade 3	453	0	0.0	0.0	0.8	153	0	0.0	0.0	2.4	155	0	0.0	0.0	2.4
	Related	453	14	3.1	1.7	5.1	153	2	1.3	0.2	4.6	155	4	2.6	0.7	6.5

N = number of subjects with a documented dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95%CI = exact 95% confidence interval; LL = lower limit, UL = upper limit
Any = occurrence of any solicited general symptom regardless of their intensity grade or relationship to the study vaccination.
Grade 3 arthralgia, fatigue, headache, gastrointestinal, myalgia, rash = symptoms that prevented normal activity
Grade 3 urticaria = urticaria distributed on at least 4 body areas
Related = general symptom assessed by the investigator as causally related to the study vaccination

Secondary Outcome Variable (s):
Occurrence of potential NOCDs (GSK assessment) up to Month 7 (Total Vaccinated Cohort)

New Onset Chronic Disease	Lot 1 Group N = 156				Lot 2 Group N = 156				Lot 3 Group N = 146			
	n	%	95% CI		n	%	95% CI		n	%	95% CI	
			LL	UL			LL	UL			LL	UL
Subjects with any NOCD(s)	4	2.6	0.7	6.4	4	2.6	0.7	6.4	7	4.8	1.9	9.6
Hypothyroidism	1	0.6	0.0	3.5	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Hypersensitivity	0	0.0	0.0	2.3	1	0.6	0.0	3.5	1	0.7	0.0	3.8
Seasonal allergy	0	0.0	0.0	2.3	1	0.6	0.0	3.5	1	0.7	0.0	3.8
Asthma	1	0.6	0.0	3.5	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Rhinitis allergic	0	0.0	0.0	2.3	1	0.6	0.0	3.5	1	0.7	0.0	3.8
Diabetes mellitus insulin-dependent	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Urticaria	1	0.6	0.0	3.5	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Urticaria chronic	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Urticaria localized	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
	Pooled_lots Group N = 458				Old_M Group N = 154				[10-14] Group N = 158			
Subjects with any NOCD(s)	15	3.3	1.8	5.3	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Hypothyroidism	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Hypersensitivity	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Seasonal allergy	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Asthma	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Rhinitis allergic	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Urticaria	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Diabetes mellitus insulin-dependent	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Urticaria chronic	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Urticaria localized	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Occurrence of NOCDs (GSK assessment) from Month 7 up to Month 12 (ESFU Vaccinated Cohort)

New Onset Chronic Disease	Lot 1 Group N = 147				Lot 2 Group N = 148				Lot 3 Group N = 145			
	n	%	95% CI		n	%	95% CI		n	%	95% CI	
			LL	UL			LL	UL			LL	UL
Subjects with any NOCD(s)	4	2.7	0.7	6.8	0	0.0	0.0	2.5	2	1.4	0.2	4.9
Angioneurotic edema	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Demyelination	0	0.0	0.0	2.5	0	0.0	0.0	2.5	1	0.7	0.0	3.8
Dermatitis atopic	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Generalised anxiety disorder	0	0.0	0.0	2.5	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Hypersensitivity	0	0.0	0.0	2.5	0	0.0	0.0	2.5	1	0.7	0.0	3.8
Nickel sensitivity	0	0.0	0.0	2.5	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Seasonal allergy	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Solar urticaria	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Thyroiditis	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5

	Pooled_lots Group N = 440				Old_M Group N = 144				[10-14] Group N = 149			
Subjects with any NOCD(s)	6	1.4	0.5	2.9	2	1.4	0.2	4.9	0	0.0	0.0	2.4
Angioneurotic oedema	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Demyelination	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Dermatitis atopic	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Generalised anxiety disorder	0	0.0	0.0	0.8	1	0.7	0.0	3.8	0	0.0	0.0	2.4
Hypersensitivity	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Nickel sensitivity	0	0.0	0.0	0.8	1	0.7	0.0	3.8	0	0.0	0.0	2.4
Seasonal allergy	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Solar urticaria	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Thyroiditis	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Occurrence of NOCDs (GSK assessment) from Month 12 up to Month 24 (Total Vaccinated Cohort)

New Onset Chronic Disease	Pooled_lots Group N = 186				Old_M Group N = 64				[10-14] Group N = 57			
	n	%	95% CI		n	%	95% CI		n	%	95% CI	
			LL	UL			LL	UL			LL	UL
Subjects with any NOCD(s)	1	0.5	0.0	3.0	0	0.0	0.0	5.6	1	1.8	0.0	9.4
Asthma	1	0.5	0.0	3.0	0	0.0	0.0	5.6	1	1.8	0.0	9.4

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Occurrence of NOCDs (GSK assessment) from Month 24 up to Month 36 (Total Vaccinated Cohort)

New Onset Chronic Disease	Pooled_lots Group N = 184				Old_M Group N = 65				[10-14] Group N = 53			
	n	%	95% CI		n	%	95% CI		n	%	95% CI	
			LL	UL			LL	UL			LL	UL
Subjects with any NOCD(s)	3	1.6	0.3	4.7	0	0.0	0.0	5.5	1	1.9	0.0	10.1
Hypothyroidism	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Coeliac disease	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Seasonal allergy	0	0.0	0.0	2.0	0	0.0	0.0	5.5	1	1.9	0.0	10.1
Rheumatoid arthritis	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Asthma	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Occurrence of NOCDs (GSK assessment) from Month 36 up to Month 48 (Total Vaccinated cohort)

New Onset Chronic Disease	Pooled_lots Group N = 169				Old_M Group N = 63				[10-14] Group N = 51			
	n	%	95% CI		n	%	95% CI		n	%	95% CI	
			LL	UL			LL	UL			LL	UL
Subjects with any NOCD(s)	0	0.0	0.0	2.2	1	1.6	0.0	8.5	1	2.0	0.0	10.4
Iritis	0	0.0	0.0	2.2	1	1.6	0.0	8.5	0	0.0	0.0	7.0
Arthritis	0	0.0	0.0	2.2	1	1.6	0.0	8.5	0	0.0	0.0	7.0
Juvenile arthritis	0	0.0	0.0	2.2	0	0.0	0.0	5.7	1	2.0	0.0	10.4

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Number (%) of subjects with medically significant adverse events within 30 days (Day 0-29) post-vaccination period (Total

Vaccinated Cohort)												
Medically significant AEs	Lot 1 Group N = 156				Lot 2 Group N = 156				Lot 3 Group N = 146			
	n	%	95% CI		n	%	95% CI		n	%	95% CI	
			LL	UL			LL	UL			LL	UL
Subjects with any medically significant AE(s)	11	7.1	3.6	12.3	13	8.3	4.5	13.8	15	10.3	5.9	16.4
Cystitis	3	1.9	0.4	5.5	1	0.6	0.0	3.5	2	1.4	0.2	4.9
Pharyngolaryngeal pain	0	0.0	0.0	2.3	0	0.0	0.0	2.3	3	2.1	0.4	5.9
Acne	0	0.0	0.0	2.3	1	0.6	0.0	3.5	1	0.7	0.0	3.8
Influenza	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Toothache	0	0.0	0.0	2.3	0	0.0	0.0	2.3	2	1.4	0.2	4.9
Chest pain	1	0.6	0.0	3.5	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Chlamydial infection	0	0.0	0.0	2.3	1	0.6	0.0	3.5	1	0.7	0.0	3.8
Dizziness	1	0.6	0.0	3.5	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Eczema	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Pyrexia	0	0.0	0.0	2.3	1	0.6	0.0	3.5	1	0.7	0.0	3.8
Salpingitis	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Seasonal allergy	1	0.6	0.0	3.5	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Tooth extraction	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Abdominal pain upper	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Anaemia	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Animal bite	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Arthritis	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Asthenia	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Bone fissure	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Bronchial irritation	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Bronchitis acute	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Bursitis	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Candidiasis	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Cough	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Dental caries	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Depression	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Diarrhea	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Ear pain	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Erythema	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Eye irritation	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Fatigue	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Foot fracture	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Forearm fracture	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Fungal infection	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Gastric ph decreased	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Gastro-esophageal reflux disease	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Genital rash	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Headache	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Hypothyroidism	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Infectious mononucleosis	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Insomnia	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Keratitis	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Malaise	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Onychalgia	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Onychomycosis	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Osteochondrosis	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Pain in extremity	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Panic disorder	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Paresthesia	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8

Photosensitivity allergic reaction	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Pneumonia	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Pneumonia chlamydial	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Respiratory tract infection viral	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Sleep disorder	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Stomach discomfort	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Syncope	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Torticollis	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Viral upper respiratory tract infection	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Vomiting	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
	Pooled_lots Group N = 458				Old_M Group N = 154				[10-14] Group N = 158			
	39	8.5	6.1	11.5	16	10.4	6.1	16.3	12	7.6	4.0	12.9
Cystitis	6	1.3	0.5	2.8	3	1.9	0.4	5.6	0	0.0	0.0	2.3
Pharyngolaryngeal pain	3	0.7	0.1	1.9	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Acne	2	0.4	0.1	1.6	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Influenza	1	0.2	0.0	1.2	2	1.3	0.2	4.6	0	0.0	0.0	2.3
Toothache	2	0.4	0.1	1.6	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Chest pain	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Chlamydial infection	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Dizziness	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Eczema	0	0.0	0.0	0.8	1	0.6	0.0	3.6	1	0.6	0.0	3.5
Pyrexia	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Salpingitis	1	0.2	0.0	1.2	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Seasonal allergy	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Tooth extraction	1	0.2	0.0	1.2	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Abdominal pain upper	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Anaemia	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Animal bite	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Arthritis	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Asthenia	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Bone fissure	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Bronchial irritation	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Bronchitis acute	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Bursitis	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Candidiasis	1	0.2	0.0	1.2	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Cough	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Dental caries	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Depression	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Diarrhoea	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Ear pain	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Erythema	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Eye irritation	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Fatigue	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Foot fracture	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Forearm fracture	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Fungal infection	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Gastric ph decreased	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Gastrooesophageal reflux disease	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Genital rash	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Headache	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Hypothyroidism	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Infectious mononucleosis	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Insomnia	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Keratitis	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3

Malaise	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Onychalgia	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Onychomycosis	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Osteochondrosis	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Pain in extremity	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Panic disorder	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Paraesthesia	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Photosensitivity allergic reaction	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Pneumonia	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Pneumonia chlamydial	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Respiratory tract infection viral	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Sleep disorder	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Stomach discomfort	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Syncope	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Torticollis	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Viral upper respiratory tract infection	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Vomiting	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Number (%) of subjects with medically significant adverse events starting from Day-30 post-vaccination up to Month 7 (Total Vaccinated Cohort)

Medically significant AEs	Lot 1 Group N = 156				Lot 2 Group N = 156				Lot 3 Group N = 146			
	n	%	95% CI		n	%	95% CI		n	%	95% CI	
			LL	UL			LL	UL			LL	UL
Subjects with any medically significant AE(s)	5	3.2	1.0	7.3	3	1.9	0.4	5.5	3	2.1	0.4	5.9
Asthma	1	0.6	0.0	3.5	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Abdominal pain	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Abortion threatened	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Acne	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Bacterial infection	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Cystitis	0	0.0	0.0	2.3	1	0.6	0.0	3.5	0	0.0	0.0	2.5
Depression	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Eczema	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Eye infection	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Hypothyroidism	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Insomnia	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Irritable bowel syndrome	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Lymphadenitis	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Neuropathy	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Pain in extremity	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Pharyngolaryngeal pain	0	0.0	0.0	2.3	0	0.0	0.0	2.3	1	0.7	0.0	3.8
Tonsillectomy	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Urticaria chronic	1	0.6	0.0	3.5	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Vaginal discharge	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
Vomiting	0	0.0	0.0	2.3	0	0.0	0.0	2.3	0	0.0	0.0	2.5
	Pooled_lots Group N = 458				Old_M Group N = 154				[10-14] Group N = 158			
	11	2.4	1.2	4.3	5	3.2	1.1	7.4	2	1.3	0.2	4.5
Asthma	2	0.4	0.1	1.6	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Abdominal pain	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Abortion threatened	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Acne	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3

Bacterial infection	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Cystitis	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Depression	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Eczema	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Eye infection	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Hypothyroidism	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Insomnia	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Irritable bowel syndrome	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Lymphadenitis	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Neuropathy	0	0.0	0.0	0.8	0	0.0	0.0	2.4	1	0.6	0.0	3.5
Pain in extremity	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Pharyngolaryngeal pain	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Tonsillectomy	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Urticaria chronic	1	0.2	0.0	1.2	0	0.0	0.0	2.4	0	0.0	0.0	2.3
Vaginal discharge	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3
Vomiting	0	0.0	0.0	0.8	1	0.6	0.0	3.6	0	0.0	0.0	2.3

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Number (%) of subjects with medically significant adverse events from Month 7 up to Month 12 (EFSU Vaccinated Cohort)

Medically significant AEs	Lot 1 Group N = 147				Lot 2 Group N = 148				Lot 3 Group N = 145			
	n	%	95% CI		n	%	95% CI		n	%	95% CI	
			LL	UL			LL	UL			LL	UL
Subjects with any medically significant AE(s)	8	5.4	2.4	10.4	5	3.4	1.1	7.7	4	2.8	0.8	6.9
Hypersensitivity	0	0.0	0.0	2.5	1	0.7	0.0	3.7	1	0.7	0.0	3.8
Alcohol poisoning	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Angioneurotic oedema	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Arrhythmia	0	0.0	0.0	2.5	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Benign breast neoplasm	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Demyelination	0	0.0	0.0	2.5	0	0.0	0.0	2.5	1	0.7	0.0	3.8
Depression	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Dermatitis atopic	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Endometriosis	0	0.0	0.0	2.5	1	0.7	0.0	3.7	0	0.0	0.0	2.5
Generalised anxiety disorder	0	0.0	0.0	2.5	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Herpes simplex	0	0.0	0.0	2.5	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Infectious mononucleosis	0	0.0	0.0	2.5	0	0.0	0.0	2.5	1	0.7	0.0	3.8
Lymphadenitis	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Migraine	0	0.0	0.0	2.5	0	0.0	0.0	2.5	1	0.7	0.0	3.8
Pertussis	0	0.0	0.0	2.5	1	0.7	0.0	3.7	0	0.0	0.0	2.5
Pneumonia	0	0.0	0.0	2.5	0	0.0	0.0	2.5	1	0.7	0.0	3.8
Pyelonephritis	0	0.0	0.0	2.5	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Red blood cell sedimentation rate increased	0	0.0	0.0	2.5	1	0.7	0.0	3.7	0	0.0	0.0	2.5
Salpingitis	0	0.0	0.0	2.5	1	0.7	0.0	3.7	0	0.0	0.0	2.5
Seasonal allergy	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Shoulder pain	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Skin cosmetic procedure	0	0.0	0.0	2.5	0	0.0	0.0	2.5	0	0.0	0.0	2.5
Thyroiditis	1	0.7	0.0	3.7	0	0.0	0.0	2.5	0	0.0	0.0	2.5
	Pooled_lots Group N = 440				Old_M Group N = 144				[10-14] Group N = 149			
	17	3.9	2.3	6.1	5	3.5	1.1	7.9	0	0.0	0.0	2.4
Hypersensitivity	2	0.5	0.1	1.6	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Alcohol poisoning	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Angioneurotic oedema	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4

Arrhythmia	0	0.0	0.0	0.8	1	0.7	0.0	3.8	0	0.0	0.0	2.4
Benign breast neoplasm	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Demyelination	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Depression	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Dermatitis atopic	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Endometriosis	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Generalised anxiety disorder	0	0.0	0.0	0.8	1	0.7	0.0	3.8	0	0.0	0.0	2.4
Herpes simplex	0	0.0	0.0	0.8	1	0.7	0.0	3.8	0	0.0	0.0	2.4
Infectious mononucleosis	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Lymphadenitis	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Migraine	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Pertussis	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Pneumonia	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Pyelonephritis	0	0.0	0.0	0.8	1	0.7	0.0	3.8	0	0.0	0.0	2.4
Red blood cell sedimentation rate increased	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Salpingitis	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Seasonal allergy	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Shoulder pain	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4
Skin cosmetic procedure	0	0.0	0.0	0.8	1	0.7	0.0	3.8	0	0.0	0.0	2.4
Thyroiditis	1	0.2	0.0	1.3	0	0.0	0.0	2.5	0	0.0	0.0	2.4

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Number (%) of subjects with medically significant adverse events from Month 12 up to Month 24 (Total Vaccinated cohort)

Medically significant AEs	Pooled_lots Group N = 186				Old_M Group N = 64				[10-14] Group N = 57			
	n	%	95% CI		n	%	95% CI		n	%	95% CI	
			LL	UL			LL	UL			LL	UL
Subjects with any medically significant AE(s)	12	6.5	3.4	11.0	4	6.3	1.7	15.2	2	3.5	0.4	12.1
Asthma	1	0.5	0.0	3.0	0	0.0	0.0	5.6	1	1.8	0.0	9.4
Depression	2	1.1	0.1	3.8	0	0.0	0.0	5.6	0	0.0	0.0	6.3
Pyelonephritis	0	0.0	0.0	2.0	2	3.1	0.4	10.8	0	0.0	0.0	6.3
Abdominal pain	0	0.0	0.0	2.0	1	1.6	0.0	8.4	0	0.0	0.0	6.3
Bulimia nervosa	0	0.0	0.0	2.0	1	1.6	0.0	8.4	0	0.0	0.0	6.3
Cervical dysplasia	1	0.5	0.0	3.0	0	0.0	0.0	5.6	0	0.0	0.0	6.3
Concussion	1	0.5	0.0	3.0	0	0.0	0.0	5.6	0	0.0	0.0	6.3
Dermatitis	1	0.5	0.0	3.0	0	0.0	0.0	5.6	0	0.0	0.0	6.3
Endometriosis	1	0.5	0.0	3.0	0	0.0	0.0	5.6	0	0.0	0.0	6.3
Epilepsy	0	0.0	0.0	2.0	0	0.0	0.0	5.6	1	1.8	0.0	9.4
Gynaecological chlamydia infection	1	0.5	0.0	3.0	0	0.0	0.0	5.6	0	0.0	0.0	6.3
Herpes simplex	1	0.5	0.0	3.0	0	0.0	0.0	5.6	0	0.0	0.0	6.3
Infectious mononucleosis	1	0.5	0.0	3.0	0	0.0	0.0	5.6	0	0.0	0.0	6.3
Ovarian cyst	1	0.5	0.0	3.0	0	0.0	0.0	5.6	0	0.0	0.0	6.3
Premature separation of placenta	1	0.5	0.0	3.0	0	0.0	0.0	5.6	0	0.0	0.0	6.3
Smear cervix abnormal	1	0.5	0.0	3.0	0	0.0	0.0	5.6	0	0.0	0.0	6.3

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Number (%) of subjects with medically significant adverse events from Month 24 up to Month 36 (Total Vaccinated cohort)

Medically significant AEs	Pooled_lots Group N = 184				Old_M Group N = 65				[10-14] Group N = 53			
	n	%	95% CI		n	%	95% CI		n	%	95% CI	
			LL	UL			LL	UL			LL	UL

Subjects with any medically significant AE(s)	35	19.0	13.6	25.4	10	15.4	7.6	26.5	6	11.3	4.3	23.0
Myocarditis	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Hypothyroidism	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Abdominal pain	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Coeliac disease	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Duodenal ulcer	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Biliary colic	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Seasonal allergy	0	0.0	0.0	2.0	0	0.0	0.0	5.5	1	1.9	0.0	10.1
Bronchitis	0	0.0	0.0	2.0	1	1.5	0.0	8.3	0	0.0	0.0	6.7
Chlamydial infection	1	0.5	0.0	3.0	1	1.5	0.0	8.3	0	0.0	0.0	6.7
Cystitis	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Fungal skin infection	0	0.0	0.0	2.0	1	1.5	0.0	8.3	0	0.0	0.0	6.7
Genital herpes	4	2.2	0.6	5.5	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Mastitis	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Oral herpes	0	0.0	0.0	2.0	1	1.5	0.0	8.3	1	1.9	0.0	10.1
Osteomyelitis	0	0.0	0.0	2.0	0	0.0	0.0	5.5	1	1.9	0.0	10.1
Otitis media	0	0.0	0.0	2.0	0	0.0	0.0	5.5	1	1.9	0.0	10.1
Pneumonia	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Overdose	0	0.0	0.0	2.0	0	0.0	0.0	5.5	1	1.9	0.0	10.1
Road traffic accident	0	0.0	0.0	2.0	0	0.0	0.0	5.5	1	1.9	0.0	10.1
Whiplash injury	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Arthroscopy	0	0.0	0.0	2.0	1	1.5	0.0	8.3	0	0.0	0.0	6.7
Smear cervix abnormal	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Arthralgia	0	0.0	0.0	2.0	2	3.1	0.4	10.7	0	0.0	0.0	6.7
Back pain	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Plica syndrome	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Rheumatoid arthritis	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Carpal tunnel syndrome	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Hypertonia	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Migraine	1	0.5	0.0	3.0	1	1.5	0.0	8.3	0	0.0	0.0	6.7
Blighted ovum	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Depression	5	2.7	0.9	6.2	2	3.1	0.4	10.7	0	0.0	0.0	6.7
Stress	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Endometriosis	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Vaginal haemorrhage	0	0.0	0.0	2.0	1	1.5	0.0	8.3	0	0.0	0.0	6.7
Asthma	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Rhinitis allergic	0	0.0	0.0	2.0	1	1.5	0.0	8.3	0	0.0	0.0	6.7
Acne	2	1.1	0.1	3.9	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Dermatitis	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Pityriasis rosea	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7
Hypertension	1	0.5	0.0	3.0	0	0.0	0.0	5.5	0	0.0	0.0	6.7

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Number (%) of subjects with medically significant adverse events from Month 36 up to Month 48 (Total Vaccinated cohort)

Medically significant AEs	Pooled_lots Group N = 169				Old_M Group N = 63				[10-14] Group N = 51			
	N	%	95% CI		n	%	95% CI		n	%	95% CI	
			LL	UL			LL	UL			LL	UL
Subjects with any medically significant AE(s)	19	11.2	6.9	17.0	5	7.9	2.6	17.6	1	2.0	0.0	10.4
Cardiac disorder	0	0.0	0.0	2.2	1	1.6	0.0	8.5	0	0.0	0.0	7.0
Iritis	0	0.0	0.0	2.2	1	1.6	0.0	8.5	0	0.0	0.0	7.0
Abdominal pain	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Diarrhoea	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0

Dyspepsia	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Candidiasis	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Cystitis	1	0.6	0.0	3.3	1	1.6	0.0	8.5	0	0.0	0.0	7.0
Genital herpes	0	0.0	0.0	2.2	1	1.6	0.0	8.5	0	0.0	0.0	7.0
Oral herpes	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Pneumonia	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Pyelonephritis	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Scarlet fever	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Viral infection	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Juvenile arthritis	0	0.0	0.0	2.2	0	0.0	0.0	5.7	1	2.0	0.0	10.4
Pain in extremity	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Abortion spontaneous	0	0.0	0.0	2.2	2	3.2	0.4	11.0	0	0.0	0.0	7.0
Chorioamnionitis	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Stillbirth	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Attention deficit/hyperactivity disorder	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Depression	3	1.8	0.4	5.1	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Endometriosis	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Ovarian cyst	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Asthma	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Acne	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0
Hypertension	1	0.6	0.0	3.3	0	0.0	0.0	5.7	0	0.0	0.0	7.0

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects reporting at least once the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Secondary Outcome Variable (s):
Outcome of reported pregnancies during the extension follow-up period from Month 12 to Month 24 (Total Vaccinated cohort)

Outcome	Pooled_lots Group	Old_M Group	[10 - 14] Group
Abnormal infant / congenital anomaly	0	0	0
Ectopic pregnancy	0	0	0
Elective termination	0	0	0
Lost to follow-up	0	0	0
Missed abortion	0	0	0
Normal infant	3	2	0
Ongoing	0	0	0
Premature birth	1	0	0
Spontaneous abortion / Miscarriage	0	0	0
Still birth	0	0	0
Therapeutic abortion	0	0	0
Total	4	2	0

Secondary Outcome Variable (s):
Outcome of reported pregnancies during the extension follow-up period from Month 24 to Month 36 (Total Vaccinated cohort)

Outcome	Pooled_lots Group	Old_M Group	[10 - 14] Group
Abnormal infant / congenital anomaly	0	0	0
Ectopic pregnancy	0	0	0
Elective termination	1	0	0
Lost to follow-up	0	0	0
Missed abortion	0	0	0
Normal infant	15	5	0
Ongoing	2	2	0
Premature birth	1	0	0
Spontaneous abortion / Miscarriage	0	0	0
Still birth	0	0	0

Therapeutic abortion	1	0	0
Total	20	7	0

Secondary Outcome Variable (s):
Outcome of reported pregnancies during the extension follow-up period from Month 36 to Month 48 (Total Vaccinated cohort)

Outcome	Pooled_lots Group N = 169	Old_M Group N = 63	[10 - 14] Group N = 51
Abnormal infant / congenital anomaly	0	0	0
Ectopic pregnancy	0	0	0
Elective termination	1	0	0
Lost to follow-up	0	0	0
Missed abortion	1	0	0
Normal infant	12	4	1
Ongoing	0	0	0
Premature birth	0	0	0
Spontaneous abortion / Miscarriage	0	2	0
Stillbirth	1	0	0
Therapeutic abortion	0	0	0
Outcome unkown	0	0	0
Total	15	6	1

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

Most frequent adverse events - On-Therapy (occurring within Day 0-29 following vaccination)	Lot 1 Group N = 156	Lot 2 Group N = 156	Lot 3 Group N = 146	Pooled_lots Group N = 458	Old_M Group N = 154	[10-14] Group N = 158
Subjects with any AE(s), n (%)	76 (48.7)	64 (41.0)	68 (46.6)	208 (45.4)	70 (45.5)	55 (34.8)
Subjects with grade 3* AE(s), n (%)	13 (8.3)	5 (3.2)	13 (8.9)	31 (6.8)	12 (7.8)	10 (6.3)
Subjects with related** AE(s), n (%)	24 (15.4)	24 (15.4)	27 (18.5)	75 (16.4)	23 (14.9)	10 (6.3)
Headache	11 (7.1)	12 (7.7)	10 (6.8)	33 (7.2)	13 (8.4)	4 (2.5)
Influenza	5 (3.2)	7 (4.5)	6 (4.1)	18 (3.9)	10 (6.5)	2 (1.3)
Pharyngolaryngeal pain	6 (3.8)	4 (2.6)	8 (5.5)	18 (3.9)	9 (5.8)	3 (1.9)
Injection site pruritus	8 (5.1)	3 (1.9)	6 (4.1)	17 (3.7)	4 (2.6)	3 (1.9)
Dysmenorrhoea	5 (3.2)	8 (5.1)	0 (0.0)	13 (2.8)	7 (4.5)	1 (0.6)
Injection site haemorrhage	2 (1.3)	8 (5.1)	3 (2.1)	13 (2.8)	5 (3.2)	1 (0.6)
Nasopharyngitis	5 (3.2)	2 (1.3)	3 (2.1)	10 (2.2)	2 (1.3)	7 (4.4)
Cough	4 (2.6)	2 (1.3)	3 (2.1)	9 (2.0)	1 (0.6)	8 (5.1)
Dizziness	2 (1.3)	2 (1.3)	6 (4.1)	10 (2.2)	2 (1.3)	2 (1.3)
Rhinitis	4 (2.6)	0 (0.0)	3 (2.1)	7 (1.5)	1 (0.6)	6 (3.8)
Upper respiratory tract infection	3 (1.9)	1 (0.6)	1 (0.7)	5 (1.1)	2 (1.3)	4 (2.5)
Injection site reaction	1 (0.6)	4 (2.6)	0 (0.0)	5 (1.1)	1 (0.6)	1 (0.6)

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

Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) up to Month 7 (Total Vaccinated Cohort)

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

All SAEs	Lot 1 Group N = 156	Lot 2 Group N = 156	Lot 3 Group N = 146	Pooled_lots Group N = 458	Old_M Group N = 154	[10-14] Group N = 158
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	2 (1.3) [0]	2 (1.3) [0]	3 (2.1) [0]	7 (1.5) [0]	0 (0.0) [0]	1 (0.6) [0]
Abortion threatened	0 (0.0) [0]	1 (0.6) [0]	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Acute sinusitis	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Diabetes mellitus insulin-dependent	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Gastric ulcer	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Heat stroke	0 (0.0) [0]	1 (0.6) [0]	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Myocarditis	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Pericarditis	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]

Depression	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.6) [0]
Fatal SAEs	Lot 1 Group N = 156	Lot 2 Group N = 156	Lot 3 Group N = 146	Pooled_lots Group N = 458	Old_M Group N = 154	[10-14] Group N = 158
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) from Month 7 up to Month 12 (EFSU Vaccinated Cohort)						
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]						
All SAEs	Lot 1 Group N = 147	Lot 2 Group N = 148	Lot 3 Group N = 145	Pooled_lots Group N = 440	Old_M Group N = 144	[10-14] Group N = 149
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	2 (1.4) [0]	1 (0.7) [0]	2 (1.4) [0]	5 (1.1) [0]	0 (0.0) [0]	0 (0.0) [0]
Lymphadenitis	1 (0.7) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Hypersensitivity	0 (0.0) [0]	1 (0.7) [0]	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Condyloma acuminatum	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Alcohol poisoning	1 (0.7) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Demyelination	0 (0.0) [0]	0 (0.0) [0]	1 (0.7) [0]	1 (0.2) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	Lot 1 Group N = 147	Lot 2 Group N = 148	Lot 3 Group N = 145	Pooled_lots Group N = 440	Old_M Group N = 144	[10-14] Group N = 149
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) from Month 12 up to Month 24 (Total Vaccinated cohort)						
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]						

All SAEs	Pooled_lots Group N = 186	Old_M Group N = 64	[10-14] Group N = 57
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	2 (1.1) [0] *	1 (1.6) [0]	0 (0.0) [0]
Pyelonephritis	0 (0.0) [0]	1 (1.6) [0]	0 (0.0) [0]
Premature separation of placenta	1 (0.5) [0]	0 (0.0) [0]	0 (0.0) [0]
Endometriosis	1 (0.5) [0]	0 (0.0) [0]	0 (0.0) [0]
Ovarian cyst	1 (0.5) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	Pooled_lots Group N = 186	Old_M Group N = 64	[10-14] Group N = 57
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
* One subject in the Pooled_lots Group experienced a long QT syndrome 12 months after receiving the third dose of vaccine. The event was assessed by the investigator as life-threatening and medically important but not possibly related to study vaccination. This SAE was not tabulated as the subject was not enrolled in the extension M24 study			
Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) from Month 24 up to Month 36 (Total Vaccinated cohort)			
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]			
All SAEs	Pooled_lots Group N = 184	Old_M Group N = 65	[10-14] Group N = 53
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	7 (3.8) [0]	0(0.0) [0]	3(5.7) [0]
Abdominal pain	1 (0.5) [0]	0(0.0) [0]	0 (0.0) [0]
Anogenital warts	1 (0.5) [0]	0(0.0) [0]	0 (0.0) [0]
Enteritis infectious	1 (0.5) [0]	0(0.0) [0]	0 (0.0) [0]
Genital herpes	1 (0.5) [0]	0(0.0) [0]	0 (0.0) [0]
Osteomyelitis	0 (0.0) [0]	0(0.0) [0]	1 (1.9) [0]
Overdose	0 (0.0) [0]	0(0.0) [0]	1 (1.9) [0]
Road traffic accident	0 (0.0) [0]	0(0.0) [0]	1 (1.9) [0]

Blighted ovum	1 (0.5) [0]	0(0.0) [0]	0 (0.0) [0]
Endometriosis	1 (0.5) [0]	0(0.0) [0]	0 (0.0) [0]
Dermatitis	1 (0.5) [0]	0(0.0) [0]	0 (0.0) [0]
Fatal SAEs	Pooled_lots Group N = 184	Old_M Group N = 65	[10-14] Group N = 53
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]
Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) from Month 36 up to Month 48 (Total Vaccinated cohort)			
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]			
All SAEs	Pooled_lots Group N = 169	Old_M Group N = 63	[10-14] Group N = 51
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	5 (3.0) [0]	2 (3.2) [0]	0 (0.0) [0]
Abortion spontaneous	0 (0.0) [0]	2 (3.2) [0]	0 (0.0) [0]
Chorioamnionitis	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Diarrhoea	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Endometriosis	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Enterocolitis infectious	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Stillbirth	1 (0.6) [0]	0 (0.0) [0]	0 (0.0) [0]
Fatal SAEs	Pooled_lots Group N = 169	Old_M Group N = 63	10-14] Group N = 51
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

Conclusion: For immunogenicity and safety results pertaining to the active phase of the study, please refer to the Pedersen (2007) publication citation.
At Month 24, Month 36 and Month 48, GMTs for anti-HPV-16 antibodies were 1440.4, 1397.5 and 1140.9 in Pooled_lots Group, 1903.7, 1679.3 and 1427.3 in Old_M Group and 3861.7, 3353.0 and 2862.2 in [10-14] Group, respectively. At Month 24, Month 36 and Month 48, GMTs for anti-HPV-18 antibodies were 649.8, 574.7 and 462.4 in Pooled_lots Group, 778.8, 649.6 and 519.9 in Old_M Group and 1341.8, 1111.0 and 935.6 in [10-14] Group, respectively.
From Month 7 up to Month 12, SAEs were reported for 5 (1.1%) subjects from the Pooled_lots Group. From Month 12 up to Month 24, SAEs were reported for 2 (1.1%) and 1 (1.6%) subjects from the Pooled_lots Group and the Old_M Group, respectively. From Month 24 up to Month 36, SAEs were reported for 7 (3.8%) and 3 (5.7%) subjects from the Pooled_lots Group and the [10-14] Group, respectively. From Month 36 up to Month 48, 5 (3.0%) subjects in the Pooled_lots Group and 2 (3.2%) subjects in the Old_M Group reported SAEs. None of the SAEs reported during the entire course of the study were assessed by the investigators as related to the study vaccination.
No fatal SAEs were reported during the entire study.

Date updated: 11-November-2014