15 November 2012
EMA/251555/2013
Committee for Medicinal Products for Human Use (CHMP)

Cervarix

(human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed))

Procedure No. EMEA/H/C/000721/P46/064

CHMP assessment report for paediatric use studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Assessment Report as adopted by the CHMP with all information of a commercially confidential nature deleted

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1. RECOMMENDATION

Based on the review of the paediatric data on safety and immunogenicity collected in study HPV-048, Mont 48, the Rapporteur considers that the benefit-risk balance for the above mentioned product remains unchanged and therefore does not require further regulatory action on the marketing authorisation for Cervarix. The SmPC and PIL remain unchanged.

The results observed at Months 7, 12, 18, 24 and 36 have been presented previously. The final study report of study HPV-048 at Month 60 is needed to fulfil commitment FUM021.

2. BACKGROUND

The HPV-048 Clinical Study Report Annex 5 (Month 48) is submitted in accordance with the requirements of Article 46 of the regulation 1901/2006.

3. SCIENTIFIC DISCUSSION

The HPV-048 PRI study report M7 and Annex Report MI2 were previously submitted in order to fulfill commitments FUM021, 021.1 and 021.2. The Annex Reports 2 (MI8), 3 (M24) and 4 (M36) were previously submitted. From the results reported at M18, M24 and M36 it is concluded that in all age groups (9-25 years) a sustained immune response against both HPV-16 and HPV-18 antigens was observed in all vaccine groups up to 36 months after the first vaccination.

The MAH submits now the results observed at Month 48 (Annex Report 5). The submission of the final report at Month 60 to fulfil commitment FUM021 is currently planned in October 2013.

Study design: please refer to the Clinical Study Report.

Study HPV048 PRI is a phase IIII, partially-blind, randomized, multi-centre, age stratified (three age strata: 9-14 years, 15-19 years and 20-25 years), dose-range study in healthy females aged 9-25 years. This study is conducted in 21 study centres in two countries (Germany and Canada).

A total of 960 were randomized (1:1:1:1) and allocated to four treatment groups (all received the HPV 16/18 vaccine at different dosages [20 µg or 40 µg of each HPV antigen] and on different schedules [0, 2-month, 0, 6-month or 0, 1 ,6 month schedule]: 240 subjects received the 40 µg/40 µg) vaccine according to a Month 0, 2 schedule (V40_02 group), 241 subjects received the 40 µg/40 µg) vaccine according to a Month 0, 6 schedule (V40_06 group), 240 subjects received the 20 µg/20 µg) vaccine according to a Month 0, 6 schedule (V20_06 group) and 239 subjects received the 20 µg/20 µg) vaccine according to the standard Month 0, 1, 6 schedule (HPV group).

A total of 668 subjects were included at the Month 48 visit of Study HPV-048 PRI: 169, 168, 167 and 164 subjects in the V40_02, V40_06, V20_06 and HPV groups, respectively.

Primary objectives

Immunogenicity

To evaluate the immunogenicity of the HPV-16/18 vaccine one month after the last dose when administered at different dosages (20 or 40 µg of each HPV antigen) and on different schedules (0, 2- or 0, 6 months) compared with the standard administered on a 3-dose schedule (0, 1, 6 months).

The primary analysis of immunogenicity was performed on the Month 48 ATP Immunogenicity cohort. The Month 48 ATP Immunogenicity cohort included all evaluable subjects (i.e. those meeting all eligibility criteria, complying with the procedures defined in the protocol, with no elimination criteria during the study) for whom data concerning immunogenicity endpoint measures were available. This included subjects who returned for blood sampling at Month 48 and for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination.

Safety

To evaluate the reactogenicity of the HPV-16/18 vaccine when administered at different dosages (20 or 40 µg of each HPV type) and on different schedules (0, 2-or 0,6-months) with respect to the occurrence, intensity and relationship to vaccination of solicited local and general symptoms reported within 7 days (Days 0 - 6) after each and any vaccination.]

The primary analysis of safety was based on the Month 48 Total Vaccinated cohort for events reported between Month 36 and Month 48. The Month 48 Total Vaccinated cohort included all vaccinated subjects who returned for the Month 48 visit. Thus, the Month 48 Total Vaccinated cohort for analysis of safety included all subjects with at least one vaccine administration documented and the Month 48 Total Vaccinated cohort for analysis of immunogenicity included vaccinated subjects who returned for blood sampling at Month 48 and for whom data concerning immunogenicity endpoint measures were available.

Assessor's preliminary note

The secondary objectives of the study are shown in the Clinical Study Report and not reproduced here. Only the outcome with respect to the primary objectives will be discussed in the current assessment report. A complete analysis will be done at the end of the study. The only relevant group is the one that receives the 20 µg/20 µg Cervarix formulation that is currently commercially available and used according to the 0, 1, 6 month vaccination schedule. The immune responses to HPV-31 and HPV-45 will be discussed at the end of the study.

Immunogenicity results

Table 17 and Table 18 show the immunogenicity results according to the ATP analysis.

Table 19 and Table 20 show the immunogenicity results in subjects aged 9-14 years and 15-25 years.

Table 21 and Table 22 show seropositivity rates and GMTs by pre-vaccination status and by age stratum (strata: 9-14, 15-19, 20-25 years).

Figure 1 and Figure 2 show the persistence of ELISA antibody titers in subjects seronegative at baseline.

Table 17 Number and percentage of subjects with an anti-HPV 16.VLP IGG concentration equal to or above the cut-off of 8 ELU/ML and GMTs (Month 48 ATP Immunogenicity Cohort)

					≥ 8 ELU/ML				GMT				
							95% CI			95% CI			
Antibody	Group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
HPV 16.VLP IGG	V40_02	S-	PRE	149	0	0.0	0.0	2.4	4.0	4.0	4.0	<8.0	<8.0
			PII(M3)	149	149	100	97.6	100	5749.0	5019.8	6584.2	233.0	45534.0
			PIII(M7)	149	149	100	97.6	100	1426.4	1222.8	1663.9	80.0	26271.0
			PIII(M12)	149	149	100	97.6	100	1004.6	856.7	1178.0	53.0	17994.0
			PIII(M18)	148	148	100	97.5	100	933.0	785.7	1108.0	32.0	11507.0
			PIII(M24)	146	146	100	97.5	100	796.4	676.6	937.4	24.0	9500.0
			PIII(M36)	147	147	100	97.5	100	688.9	586.2	809.7	29.0	10491.0
			PIII(M48)	149	149	100	97.6	100	644.4	548.4	757.2	21.0	6475.0
		S+	PRE	11	11	100	71.5	100	34.3	15.6	75.7	9.0	413.0
			PII(M3)	11	11	100	71.5	100	5199.7	2925.5	9241.8	1744.0	20636.0
			PIII(M7)	11	11	100	71.5	100	1893.9	989.4	3625.2	521.0	11429.0
			PIII(M12)	11	11	100	71.5	100	1407.5	770.5	2571.2	338.0	7667.0
			PIII(M18)	10	10	100	69.2	100	1155.4	597.3	2235.0	281.0	5156.0
			PIII(M24)	9	9	100	66.4	100	824.1	371.3	1829.3	184.0	6264.0
			PIII(M36)	10	10	100	69.2	100	737.6	343.2	1585.5	120.0	5741.0
			PIII(M48)	11	11	100	71.5	100	723.2	361.1	1448.1	101.0	4785.0
		Total	PRE	160	11	6.9	3.5	12.0	4.6	4.2	5.1	<8.0	413.0
			PII(M3)	160	160	100	97.7	100	5709.4	5010.2	6506.3	233.0	45534.0
			PIII(M7)	160	160	100	97.7	100	1454.5	1253.6	1687.6	80.0	26271.0
			PIII(M12)	160	160	100	97.7	100	1028.1	882.4	1198.0	53.0	17994.0
			PIII(M18)	158	158	100	97.7	100	945.8	802.1	1115.1	32.0	11507.0
			PIII(M24)	155	155	100	97.6	100	798.0	681.4	934.5	24.0	9500.0
			PIII(M36)	157	157	100	97.7	100	691.9	591.7	809.1	29.0	10491.0
			PIII(M48)	160	160	100	97.7	100	649.5	556.0	758.8	21.0	6475.0
	V40_06	S-	PRE	130	0	0.0	0.0	2.8	4.0	4.0	4.0	<8.0	<8.0
			PII(M3)	130	130	100	97.2	100	351.5	294.1	420.0	43.0	7324.0
			PIII(M7)	130	130	100	97.2	100	12759.0	11105.1	14659.2	1211.0	57135.0
			PIII(M12)	129	129	100	97.2	100	3635.4	3138.9	4210.4	109.0	30300.0
			PIII(M18)	127	127	100	97.1	100	2427.8	2096.5	2811.5	107.0	15410.0
			PIII(M24)	126	126	100	97.1	100	1853.9	1605.1	2141.2	138.0	11571.0
			PIII(M36)	128	128	100	97.2	100	1540.3	1344.3	1764.9	239.0	8472.0
			PIII(M48)	130	130	100	97.2	100	1295.1	1126.3	1489.2	178.0	11546.0
		S+	PRE	21	21	100	83.9	100	62.7	33.9	116.0	10.0	594.0
			PII(M3)	21	21	100	83.9	100	1533.4	810.9	2899.6	139.0	11769.0
			PIII(M7)	21	21	100	83.9	100	6877.6	4692.3	10080.5	1534.0	33723.0
			PIII(M12)	21	21	100	83.9	100	2811.2	1942.5	4068.2	499.0	11023.0
			PIII(M18)	21	21	100	83.9	100	1979.8	1295.2	3026.3	284.0	8045.0
			PIII(M24)	21	21	100	83.9	100	1579.3	1047.5	2381.1	288.0	6774.0
			PIII(M36)	21	21	100	83.9	100	1246.6	824.2	1885.6	157.0	7224.0
			PIII(M48)	21	21	100	83.9	100	1070.2	718.6	1593.8	147.0	6467.0
		Total	PRE	151	21	13.9	8.8	20.5	5.9	4.9	7.0	<8.0	594.0
			PII(M3)	151	151	100	97.6	100	431.4	355.9	522.8	43.0	11769.0

					≥ 8 ELU/ML				GMT				
							95% CI			95% CI			
Antibody	Group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
			PIII(M7)	151	151	100	97.6	100	11708.2	10243.8	13382.1	1211.0	57135.0
			PIII(M12)	150	150	100	97.6	100	3506.9	3062.0	4016.4	109.0	30300.0
			PIII(M18)	148	148	100	97.5	100	2358.6	2054.6	2707.6	107.0	15410.0
			PIII(M24)	147	147	100	97.5	100	1811.9	1583.0	2073.9	138.0	11571.0
			PIII(M36)	149	149	100	97.6	100	1495.1	1313.9	1701.2	157.0	8472.0
			PIII(M48)	151	151	100	97.6	100	1261.2	1106.4	1437.7	147.0	11546.0
	V20_06	S-	PRE	139	0	0.0	0.0	2.6	4.0	4.0	4.0	<8.0	<8.0
			PII(M3)	139	139	100	97.4	100	250.7	209.7	299.7	25.0	7463.0
			PIII(M7)	139	139	100	97.4	100	8675.3	7505.6	10027.3	973.0	60582.0
			PIII(M12)	139	139	100	97.4	100	2600.1	2256.5	2996.0	290.0	21151.0
			PIII(M18)	138	138	100	97.4	100	1757.3	1518.0	2034.2	159.0	12109.0
			PIII(M24)	136	136	100	97.3	100	1354.7	1175.3	1561.4	149.0	7638.0
			PIII(M36)	136	136	100	97.3	100	1116.6	968.4	1287.5	88.0	7249.0
			PIII(M48)	139	139	100	97.4	100	968.5	840.6	1115.9	85.0	7307.0
		S+	PRE	18	18	100	81.5	100	40.9	23.3	71.8	9.0	337.0
			PII(M3)	18	18	100	81.5	100	1441.1	793.6	2616.8	177.0	9225.0
			PIII(M7)	18	18	100	81.5	100	5061.7	3492.4	7336.2	1479.0	26064.0
			PIII(M12)	18	18	100	81.5	100	2326.9	1624.8	3332.4	970.0	12549.0
			PIII(M18)	18	18	100	81.5	100	1589.6	1082.1	2334.9	628.0	6867.0
			PIII(M24)	18	18	100	81.5	100	1199.3	792.5	1815.1	384.0	7343.0
			PIII(M36)	17	17	100	80.5	100	982.9	647.4	1492.3	360.0	5553.0
			PIII(M48)	18	18	100	81.5	100	845.3	568.7	1256.5	334.0	4949.0
		Total	PRE	157	18	11.5	6.9	17.5	5.2	4.6	6.0	<8.0	337.0
			PII(M3)	157	157	100	97.7	100	306.3	253.0	370.9	25.0	9225.0
			PIII(M7)	157	157	100	97.7	100	8155.7	7114.8	9348.7	973.0	60582.0
			PIII(M12)	157	157	100	97.7	100	2567.2	2252.1	2926.3	290.0	21151.0
			PIII(M18)	156	156	100	97.7	100	1737.0	1516.8	1989.2	159.0	12109.0
			PIII(M24)	154	154	100	97.6	100	1335.5	1169.2	1525.5	149.0	7638.0
			PIII(M36)	153	153	100	97.6	100	1100.9	963.5	1258.0	88.0	7249.0
			PIII(M48)	157	157	100	97.7	100	953.5	835.5	1088.2	85.0	7307.0
	HPV	S-	PRE	129	0	0.0	0.0	2.8	4.0	4.0	4.0	<8.0	<8.0
			PIII(M7)	129	129	100	97.2	100	15177.0	12640.2	18223.0	1322.0	149951.0
			PIII(M12)	128	128	100	97.2	100	5131.1	4207.5	6257.4	182.0	81240.0
			PIII(M18)	128	128	100	97.2	100	3380.3	2791.2	4093.7	116.0	45075.0
			PIII(M24)	127	127	100	97.1	100	2617.3	2156.2	3176.8	112.0	35172.0
			PIII(M36)	129	129	100	97.2	100	2228.8	1847.5	2688.7	73.0	30440.0
			PIII(M48)	129	129	100	97.2	100	1825.7	1518.3	2195.5	71.0	17426.0
		S+	PRE	19	19	100	82.4	100	27.7	14.9	51.4	9.0	745.0
			PIII(M7)	19	19	100	82.4	100	11633.1	6832.7	19805.8	2482.0	99665.0
			PIII(M12)	19	19	100	82.4	100	5268.7	3175.6	8741.7	1156.0	51632.0
			PIII(M18)	19	19	100	82.4	100	3947.4	2422.4	6432.3	951.0	52061.0
			PIII(M24)	19	19	100	82.4	100	3150.7	1939.1	5119.5	812.0	37420.0
			PIII(M36)	19	19	100	82.4	100	2857.9	1750.4	4665.9	621.0	36109.0
			PIII(M48)	19	19	100	82.4	100	2413.0	1472.3	3954.7	515.0	26218.0
		Total	PRE	148	19	12.8	7.9	19.3	5.1	4.5	5.8	<8.0	745.0
			PIII(M7)	148	148	100	97.5	100	14667.6	12353.7	17414.9	1322.0	149951.0
			PIII(M12)	147	147	100	97.5	100	5148.7	4289.0	6180.6	182.0	81240.0
			PIII(M18)	147	147	100	97.5	100	3448.7	2890.8	4114.3	116.0	52061.0
			PIII(M24)	146	146	100	97.5	100	2681.2	2243.4	3204.4	112.0	37420.0
			PIII(M36)	148	148	100	97.5	100	2301.0	1934.1	2737.6	73.0	36109.0
			PIII(M48)	148	148	100	97.5	100	1892.3	1594.2	2246.0	71.0	26218.0

V40_02 = HPV-16/18(40,40) AS04 0,2 m

V40_06 = HPV-16/18(40,40) AS04 0,6m
V20_06 = HPV-16/18(20,20) AS04 0,6 m
HPV = HPV-16/18(20,20) AS04 0,1,6m
S- = seronegative subjects (antibody concentration < 8 ELU/ML) prior to vaccination
S+ = seropositive subjects (antibody concentration ≥ 8 ELU/ML) prior to vaccination
GMT = geometric mean titers concentration calculated on all subjects
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with concentration equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = pre-vaccination
PII(M3) = Post Dose II, Month 3
PIII(M7) = Post Dose III, Month 7
PIII(M12) = Post Dose III, Month 12
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

Table 18 Number and percentage of subjects with an anti-HPV 18.VLP IGG concentration equal to or above the cut-off of 7 ELU/ML and GMTs (Month 48 ATP Immunogenicity Cohort)

					≥ 7 ELU/ML				GMT				
							95% CI			95% CI			
Antibody	Group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
HPV 18.VLP IGG	V40_02	S-	PRE	138	0	0.0	0.0	2.6	3.5	3.5	3.5	<7.0	<7.0
			PII(M3)	138	138	100	97.4	100	3652.7	3121.3	4274.7	148.0	33045.0
			PIII(M7)	138	138	100	97.4	100	794.5	673.3	937.4	69.0	7965.0
			PIII(M12)	138	138	100	97.4	100	436.0	365.7	520.0	25.0	5521.0
			PIII(M18)	136	136	100	97.3	100	356.7	299.3	425.2	15.0	3262.0
			PIII(M24)	133	133	100	97.3	100	305.8	255.5	366.1	12.0	3257.0
			PIII(M36)	135	135	100	97.3	100	294.0	243.5	354.9	10.0	6446.0
			PIII(M48)	138	138	100	97.4	100	256.0	212.2	308.9	9.0	5240.0
		S+	PRE	22	22	100	84.6	100	20.9	12.6	34.8	7.0	510.0
			PII(M3)	22	22	100	84.6	100	3415.7	2300.5	5071.5	671.0	33321.0
			PIII(M7)	22	22	100	84.6	100	938.2	611.0	1440.5	155.0	7467.0
			PIII(M12)	22	22	100	84.6	100	516.0	325.5	817.8	84.0	3415.0
			PIII(M18)	22	22	100	84.6	100	447.0	277.3	720.6	63.0	3091.0
			PIII(M24)	22	22	100	84.6	100	413.6	256.8	666.2	46.0	2332.0
			PIII(M36)	22	22	100	84.6	100	324.5	195.5	538.7	35.0	2081.0
			PIII(M48)	22	22	100	84.6	100	289.3	171.2	488.8	28.0	2353.0
		Total	PRE	160	22	13.8	8.8	20.1	4.5	4.0	5.0	<7.0	510.0
			PII(M3)	160	160	100	97.7	100	3619.2	3132.1	4182.1	148.0	33321.0
			PIII(M7)	160	160	100	97.7	100	812.8	697.6	947.1	69.0	7965.0
			PIII(M12)	160	160	100	97.7	100	446.3	379.2	525.2	25.0	5521.0
			PIII(M18)	158	158	100	97.7	100	368.1	312.6	433.5	15.0	3262.0
			PIII(M24)	155	155	100	97.6	100	319.2	270.0	377.4	12.0	3257.0
			PIII(M36)	157	157	100	97.7	100	298.1	250.2	355.0	10.0	6446.0
			PIII(M48)	160	160	100	97.7	100	260.4	218.5	310.2	9.0	5240.0
	V40_06	S-	PRE	139	0	0.0	0.0	2.6	3.5	3.5	3.5	<7.0	<7.0
			PII(M3)	139	139	100	97.4	100	222.9	187.4	265.2	13.0	7952.0
			PIII(M7)	139	139	100	97.4	100	6779.5	5858.7	7845.0	412.0	91976.0
			PIII(M12)	138	138	100	97.4	100	1878.5	1593.2	2214.7	190.0	34743.0
			PIII(M18)	137	137	100	97.3	100	1086.3	913.0	1292.5	102.0	19845.0
			PIII(M24)	136	136	100	97.3	100	847.4	714.3	1005.3	73.0	15066.0
			PIII(M36)	137	137	100	97.3	100	719.9	607.3	853.2	50.0	15050.0
			PIII(M48)	139	139	100	97.4	100	607.5	512.8	719.6	45.0	10456.0
		S+	PRE	14	14	100	76.8	100	24.8	11.8	52.1	8.0	387.0
			PII(M3)	14	14	100	76.8	100	1065.9	450.2	2523.4	152.0	23563.0
			PIII(M7)	14	14	100	76.8	100	6768.3	3639.8	12585.8	619.0	25115.0
			PIII(M12)	14	14	100	76.8	100	2571.7	1335.8	4951.1	240.0	9748.0
			PIII(M18)	13	13	100	75.3	100	1560.1	760.8	3199.2	218.0	7798.0
			PIII(M24)	13	13	100	75.3	100	1357.2	674.4	2731.4	155.0	8456.0
			PIII(M36)	14	14	100	76.8	100	1009.4	483.8	2106.1	116.0	6960.0
			PIII(M48)	14	14	100	76.8	100	848.2	414.2	1737.3	95.0	6170.0
		Total	PRE	153	14	9.2	5.1	14.9	4.2	3.8	4.7	<7.0	387.0
			PII(M3)	153	153	100	97.6	100	257.2	213.4	310.1	13.0	23563.0
			PIII(M7)	153	153	100	97.6	100	6778.4	5883.2	7810.0	412.0	91976.0
			PIII(M12)	152	152	100	97.6	100	1933.6	1648.9	2267.4	190.0	34743.0
			PIII(M18)	150	150	100	97.6	100	1120.9	947.2	1326.6	102.0	19845.0
			PIII(M24)	149	149	100	97.6	100	883.0	747.9	1042.5	73.0	15066.0
			PIII(M36)	151	151	100	97.6	100	742.8	629.1	877.1	50.0	15050.0
			PIII(M48)	153	153	100	97.6	100	626.3	531.0	738.7	45.0	10456.0

					≥ 7 ELU/ML				GMT				
							95% CI			95% CI			
Antibody	Group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
	V20_06	S-	PRE	135	0	0.0	0.0	2.7	3.5	3.5	3.5	<7.0	<7.0
			PII(M3)	135	135	100	97.3	100	183.7	151.6	222.7	16.0	5333.0
			PIII(M7)	135	135	100	97.3	100	5295.2	4633.1	6051.9	551.0	36047.0
			PIII(M12)	135	135	100	97.3	100	1493.7	1271.6	1754.7	99.0	11420.0
			PIII(M18)	135	135	100	97.3	100	911.2	773.4	1073.5	45.0	5847.0
			PIII(M24)	132	132	100	97.2	100	717.5	609.3	845.0	43.0	4669.0
			PIII(M36)	132	132	100	97.2	100	628.9	530.1	746.3	30.0	5844.0
			PIII(M48)	135	135	100	97.3	100	529.6	448.6	625.1	33.0	3668.0
		S+	PRE	22	22	100	84.6	100	20.6	13.0	32.8	7.0	141.0
			PII(M3)	22	22	100	84.6	100	414.1	240.8	711.9	98.0	4199.0
			PIII(M7)	22	22	100	84.6	100	4798.1	3491.0	6594.7	1851.0	18651.0
			PIII(M12)	22	22	100	84.6	100	1462.6	1055.7	2026.3	499.0	7031.0
			PIII(M18)	21	21	100	83.9	100	874.9	629.1	1216.6	258.0	3527.0
			PIII(M24)	22	22	100	84.6	100	687.1	514.1	918.2	209.0	2956.0
			PIII(M36)	21	21	100	83.9	100	564.7	411.5	774.9	152.0	2292.0
			PIII(M48)	22	22	100	84.6	100	446.1	336.2	592.0	155.0	1568.0
		Total	PRE	157	22	14.0	9.0	20.4	4.5	4.0	5.0	<7.0	141.0
			PII(M3)	157	157	100	97.7	100	205.9	171.1	247.7	16.0	5333.0
			PIII(M7)	157	157	100	97.7	100	5222.6	4622.5	5900.5	551.0	36047.0
			PIII(M12)	157	157	100	97.7	100	1489.3	1288.8	1721.1	99.0	11420.0
			PIII(M18)	156	156	100	97.7	100	906.2	782.0	1050.2	45.0	5847.0
			PIII(M24)	154	154	100	97.6	100	713.1	616.8	824.5	43.0	4669.0
			PIII(M36)	153	153	100	97.6	100	619.7	531.9	722.0	30.0	5844.0
			PIII(M48)	157	157	100	97.7	100	517.0	446.2	599.1	33.0	3668.0
	HPV	S-	PRE	129	0	0.0	0.0	2.8	3.5	3.5	3.5	<7.0	<7.0
			PIII(M7)	129	129	100	97.2	100	5640.7	4801.1	6627.2	1030.0	69885.0
			PIII(M12)	128	128	100	97.2	100	1885.0	1559.3	2278.8	167.0	26768.0
			PIII(M18)	128	128	100	97.2	100	1223.5	1015.4	1474.2	65.0	19963.0
			PIII(M24)	127	127	100	97.1	100	984.8	814.8	1190.3	39.0	13295.0
			PIII(M36)	129	129	100	97.2	100	879.2	727.9	1062.0	25.0	9702.0
			PIII(M48)	129	129	100	97.2	100	721.7	599.4	868.8	18.0	7320.0
		S+	PRE	19	19	100	82.4	100	15.0	10.3	21.8	7.0	130.0
			PIII(M7)	19	19	100	82.4	100	4687.5	2814.7	7806.4	926.0	81284.0
			PIII(M12)	19	19	100	82.4	100	1727.0	993.5	3001.8	363.0	47033.0
			PIII(M18)	19	19	100	82.4	100	1235.3	719.5	2121.0	197.0	29745.0
			PIII(M24)	19	19	100	82.4	100	943.6	540.2	1648.0	176.0	24394.0
			PIII(M36)	19	19	100	82.4	100	900.2	514.4	1575.2	206.0	24703.0
			PIII(M48)	19	19	100	82.4	100	733.8	415.4	1296.0	168.0	21133.0
		Total	PRE	148	19	12.8	7.9	19.3	4.2	3.9	4.6	<7.0	130.0
			PIII(M7)	148	148	100	97.5	100	5508.2	4727.1	6418.4	926.0	81284.0
			PIII(M12)	147	147	100	97.5	100	1863.8	1560.6	2225.9	167.0	47033.0
			PIII(M18)	147	147	100	97.5	100	1225.0	1029.1	1458.3	65.0	29745.0
			PIII(M24)	146	146	100	97.5	100	979.4	820.0	1169.7	39.0	24394.0
			PIII(M36)	148	148	100	97.5	100	881.9	738.8	1052.8	25.0	24703.0
			PIII(M48)	148	148	100	97.5	100	723.2	607.2	861.4	18.0	21133.0

V40_02 = HPV-16/18(40,40) AS04 0,2 m
V40_06 = HPV-16/18(40,40) AS04 0,6m
V20_06 = HPV-16/18(20,20) AS04 0,6 m
HPV = HPV-16/18(20,20) AS04 0,1,6m
S- = seronegative subjects (antibody concentration < 7 ELU/ML) prior to vaccination
S+ = seropositive subjects (antibody concentration ≥ 7 ELU/ML) prior to vaccination
GMT = geometric mean titers concentration calculated on all subjects

Table 19 Number and percentage of subjects with an anti-HPV 16.VLP IGG concentration equal to or above the cut-off of 8 ELU/ML and GMTs in subjects aged 9-14 years and 15-25 years (Month 48 ATP Immunogenicity Cohort)

						≥ 8 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
HPV 16.VLP IGG	V40_02	9_14	S-	PRE	61	0	0.0	0.0	5.9	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	61	61	100	94.1	100	7233.1	5876.8	8902.6	966.0	45534.0
				PIII(M7)	61	61	100	94.1	100	2011.9	1578.3	2564.7	208.0	26271.0
				PIII(M12)	61	61	100	94.1	100	1434.5	1114.6	1846.3	143.0	17994.0
				PIII(M18)	60	60	100	94.0	100	1385.7	1064.0	1804.7	138.0	11507.0
				PIII(M24)	60	60	100	94.0	100	1158.6	898.8	1493.6	124.0	9500.0
				PIII(M36)	60	60	100	94.0	100	996.3	777.5	1276.6	117.0	10491.0
				PIII(M48)	61	61	100	94.1	100	908.6	721.4	1144.3	100.0	6475.0
			Total	PRE	61	0	0.0	0.0	5.9	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	61	61	100	94.1	100	7233.1	5876.8	8902.6	966.0	45534.0
				PIII(M7)	61	61	100	94.1	100	2011.9	1578.3	2564.7	208.0	26271.0
				PIII(M12)	61	61	100	94.1	100	1434.5	1114.6	1846.3	143.0	17994.0
				PIII(M18)	60	60	100	94.0	100	1385.7	1064.0	1804.7	138.0	11507.0
				PIII(M24)	60	60	100	94.0	100	1158.6	898.8	1493.6	124.0	9500.0
				PIII(M36)	60	60	100	94.0	100	996.3	777.5	1276.6	117.0	10491.0
				PIII(M48)	61	61	100	94.1	100	908.6	721.4	1144.3	100.0	6475.0
		15_25	S-	PRE	88	0	0.0	0.0	4.1	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	88	88	100	95.9	100	4903.0	4117.9	5837.7	233.0	22930.0
				PIII(M7)	88	88	100	95.9	100	1123.9	932.1	1355.0	80.0	6111.0
				PIII(M12)	88	88	100	95.9	100	784.8	647.3	951.4	53.0	4466.0
				PIII(M18)	88	88	100	95.9	100	712.5	576.4	880.7	32.0	5415.0
				PIII(M24)	86	86	100	95.8	100	613.1	502.9	747.5	24.0	2959.0
				PIII(M36)	87	87	100	95.8	100	534.2	437.7	652.0	29.0	2701.0
				PIII(M48)	88	88	100	95.9	100	507.8	411.3	626.9	21.0	3403.0
			S+	PRE	11	11	100	71.5	100	34.3	15.6	75.7	9.0	413.0
				PII(M3)	11	11	100	71.5	100	5199.7	2925.5	9241.8	1744.0	20636.0
				PIII(M7)	11	11	100	71.5	100	1893.9	989.4	3625.2	521.0	11429.0
				PIII(M12)	11	11	100	71.5	100	1407.5	770.5	2571.2	338.0	7667.0
				PIII(M18)	10	10	100	69.2	100	1155.4	597.3	2235.0	281.0	5156.0
				PIII(M24)	9	9	100	66.4	100	824.1	371.3	1829.3	184.0	6264.0
				PIII(M36)	10	10	100	69.2	100	737.6	343.2	1585.5	120.0	5741.0
				PIII(M48)	11	11	100	71.5	100	723.2	361.1	1448.1	101.0	4785.0
			Total	PRE	99	11	11.1	5.7	19.0	5.1	4.4	5.9	<8.0	413.0
				PII(M3)	99	99	100	96.3	100	4935.1	4188.0	5815.3	233.0	22930.0
				PIII(M7)	99	99	100	96.3	100	1191.0	994.8	1425.8	80.0	11429.0
				PIII(M12)	99	99	100	96.3	100	837.4	696.8	1006.4	53.0	7667.0
				PIII(M18)	98	98	100	96.3	100	748.5	612.7	914.5	32.0	5415.0
				PIII(M24)	95	95	100	96.2	100	630.5	521.3	762.6	24.0	6264.0
				PIII(M36)	97	97	100	96.3	100	552.3	456.2	668.6	29.0	5741.0
				PIII(M48)	99	99	100	96.3	100	528.1	432.7	644.7	21.0	4785.0
	V40_06	9_14	S-	PRE	49	0	0.0	0.0	7.3	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	49	49	100	92.7	100	374.2	281.1	498.2	43.0	7324.0
				PIII(M7)	49	49	100	92.7	100	17103.0	13939.1	20985.1	2713.0	57135.0
				PIII(M12)	49	49	100	92.7	100	4465.5	3538.0	5636.2	877.0	30300.0
				PIII(M18)	49	49	100	92.7	100	2931.7	2338.4	3675.4	600.0	12570.0

						≥ 8 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M24)	48	48	100	92.6	100	2153.3	1711.2	2709.5	341.0	9840.0
				PIII(M36)	49	49	100	92.7	100	1743.3	1397.8	2174.2	239.0	8472.0
				PIII(M48)	49	49	100	92.7	100	1552.6	1218.5	1978.3	202.0	11546.0
			Total	PRE	49	0	0.0	0.0	7.3	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	49	49	100	92.7	100	374.2	281.1	498.2	43.0	7324.0
				PIII(M7)	49	49	100	92.7	100	17103.0	13939.1	20985.1	2713.0	57135.0
				PIII(M12)	49	49	100	92.7	100	4465.5	3538.0	5636.2	877.0	30300.0
				PIII(M18)	49	49	100	92.7	100	2931.7	2338.4	3675.4	600.0	12570.0
				PIII(M24)	48	48	100	92.6	100	2153.3	1711.2	2709.5	341.0	9840.0
				PIII(M36)	49	49	100	92.7	100	1743.3	1397.8	2174.2	239.0	8472.0
				PIII(M48)	49	49	100	92.7	100	1552.6	1218.5	1978.3	202.0	11546.0
		15_25	S-	PRE	81	0	0.0	0.0	4.5	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	81	81	100	95.5	100	338.4	268.3	426.6	45.0	5303.0
				PIII(M7)	81	81	100	95.5	100	10686.5	8949.7	12760.3	1211.0	48115.0
				PIII(M12)	80	80	100	95.5	100	3205.1	2657.2	3866.0	109.0	20072.0
				PIII(M18)	78	78	100	95.4	100	2156.6	1781.3	2611.0	107.0	15410.0
				PIII(M24)	78	78	100	95.4	100	1690.7	1403.9	2036.0	138.0	11571.0
				PIII(M36)	79	79	100	95.4	100	1426.5	1198.2	1698.3	283.0	7742.0
				PIII(M48)	81	81	100	95.5	100	1160.5	979.9	1374.3	178.0	5176.0
			S+	PRE	21	21	100	83.9	100	62.7	33.9	116.0	10.0	594.0
				PII(M3)	21	21	100	83.9	100	1533.4	810.9	2899.6	139.0	11769.0
				PIII(M7)	21	21	100	83.9	100	6877.6	4692.3	10080.5	1534.0	33723.0
				PIII(M12)	21	21	100	83.9	100	2811.2	1942.5	4068.2	499.0	11023.0
				PIII(M18)	21	21	100	83.9	100	1979.8	1295.2	3026.3	284.0	8045.0
				PIII(M24)	21	21	100	83.9	100	1579.3	1047.5	2381.1	288.0	6774.0
				PIII(M36)	21	21	100	83.9	100	1246.6	824.2	1885.6	157.0	7224.0
				PIII(M48)	21	21	100	83.9	100	1070.2	718.6	1593.8	147.0	6467.0
			Total	PRE	102	21	20.6	13.2	29.7	7.0	5.5	9.0	<8.0	594.0
				PII(M3)	102	102	100	96.4	100	461.8	359.2	593.7	45.0	11769.0
				PIII(M7)	102	102	100	96.4	100	9759.5	8298.8	11477.4	1211.0	48115.0
				PIII(M12)	101	101	100	96.4	100	3118.9	2645.5	3677.0	109.0	20072.0
				PIII(M18)	99	99	100	96.3	100	2117.8	1783.2	2515.3	107.0	15410.0
				PIII(M24)	99	99	100	96.3	100	1666.4	1410.2	1969.2	138.0	11571.0
				PIII(M36)	100	100	100	96.4	100	1386.7	1182.0	1626.8	157.0	7742.0
				PIII(M48)	102	102	100	96.4	100	1141.3	978.2	1331.5	147.0	6467.0
	V20_06	9_14	S-	PRE	53	0	0.0	0.0	6.7	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	53	53	100	93.3	100	274.0	211.8	354.5	73.0	6037.0
				PIII(M7)	53	53	100	93.3	100	12008.8	9732.2	14817.9	2687.0	60582.0
				PIII(M12)	53	53	100	93.3	100	3542.6	2932.6	4279.5	737.0	21151.0
				PIII(M18)	53	53	100	93.3	100	2351.2	1926.8	2869.0	529.0	10395.0
				PIII(M24)	52	52	100	93.2	100	1813.2	1489.3	2207.7	452.0	7302.0
				PIII(M36)	51	51	100	93.0	100	1530.8	1246.5	1880.0	356.0	7249.0
				PIII(M48)	53	53	100	93.3	100	1319.8	1084.1	1606.7	360.0	7307.0
			S+	PRE	2	2	100	15.8	100	10.8	1.0	111.9	9.0	13.0
				PII(M3)	2	2	100	15.8	100	216.6	16.7	2812.8	177.0	265.0
				PIII(M7)	2	2	100	15.8	100	10464.9	271.6	403258.3	7851.0	13949.0
				PIII(M12)	2	2	100	15.8	100	2833.5	246.4	32584.4	2338.0	3434.0
				PIII(M18)	2	2	100	15.8	100	2002.8	878.4	4566.4	1877.0	2137.0
				PIII(M24)	2	2	100	15.8	100	1021.0	188.9	5519.7	894.0	1166.0
				PIII(M36)	2	2	100	15.8	100	810.1	71.2	9219.5	669.0	981.0
				PIII(M48)	2	2	100	15.8	100	580.2	395.5	851.2	563.0	598.0

						≥ 8 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
			Total	PRE	55	2	3.6	0.4	12.5	4.1	3.9	4.4	<8.0	13.0
				PII(M3)	55	55	100	93.5	100	271.7	211.9	348.2	73.0	6037.0
				PIII(M7)	55	55	100	93.5	100	11948.9	9753.8	14637.9	2687.0	60582.0
				PIII(M12)	55	55	100	93.5	100	3513.9	2927.7	4217.5	737.0	21151.0
				PIII(M18)	55	55	100	93.5	100	2337.5	1929.6	2831.7	529.0	10395.0
				PIII(M24)	54	54	100	93.4	100	1775.1	1465.3	2150.3	452.0	7302.0
				PIII(M36)	53	53	100	93.3	100	1494.5	1222.8	1826.5	356.0	7249.0
				PIII(M48)	55	55	100	93.5	100	1280.9	1055.1	1555.0	360.0	7307.0
		15_25	S-	PRE	86	0	0.0	0.0	4.2	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	86	86	100	95.8	100	237.3	185.8	303.0	25.0	7463.0
				PIII(M7)	86	86	100	95.8	100	7100.0	5898.0	8546.9	973.0	47872.0
				PIII(M12)	86	86	100	95.8	100	2148.8	1779.1	2595.3	290.0	13560.0
				PIII(M18)	85	85	100	95.8	100	1465.5	1205.0	1782.3	159.0	12109.0
				PIII(M24)	84	84	100	95.7	100	1130.9	937.4	1364.4	149.0	7638.0
				PIII(M36)	85	85	100	95.8	100	924.0	769.6	1109.4	88.0	5658.0
				PIII(M48)	86	86	100	95.8	100	800.3	664.7	963.6	85.0	6368.0
			S+	PRE	16	16	100	79.4	100	48.4	27.1	86.2	11.0	337.0
				PII(M3)	16	16	100	79.4	100	1826.3	1047.9	3182.9	377.0	9225.0
				PIII(M7)	16	16	100	79.4	100	4622.4	3123.6	6840.5	1479.0	26064.0
				PIII(M12)	16	16	100	79.4	100	2270.4	1512.8	3407.2	970.0	12549.0
				PIII(M18)	16	16	100	79.4	100	1544.3	998.7	2388.0	628.0	6867.0
				PIII(M24)	16	16	100	79.4	100	1223.7	764.2	1959.5	384.0	7343.0
				PIII(M36)	15	15	100	78.2	100	1008.6	625.9	1625.3	360.0	5553.0
				PIII(M48)	16	16	100	79.4	100	886.1	567.6	1383.2	334.0	4949.0
			Total	PRE	102	16	15.7	9.2	24.2	5.9	4.9	7.2	<8.0	337.0
				PII(M3)	102	102	100	96.4	100	326.8	250.9	425.8	25.0	9225.0
				PIII(M7)	102	102	100	96.4	100	6637.7	5609.2	7854.9	973.0	47872.0
				PIII(M12)	102	102	100	96.4	100	2167.4	1830.6	2566.2	290.0	13560.0
				PIII(M18)	101	101	100	96.4	100	1477.7	1239.6	1761.6	159.0	12109.0
				PIII(M24)	100	100	100	96.4	100	1145.3	964.9	1359.4	149.0	7638.0
				PIII(M36)	100	100	100	96.4	100	936.3	791.6	1107.4	88.0	5658.0
				PIII(M48)	102	102	100	96.4	100	813.2	687.1	962.5	85.0	6368.0
	HPV	9_14	S-	PRE	49	0	0.0	0.0	7.3	4.0	4.0	4.0	<8.0	<8.0
				PIII(M7)	49	49	100	92.7	100	22772.7	17551.7	29546.9	3932.0	149951.0
				PIII(M12)	49	49	100	92.7	100	7886.0	5787.4	10745.4	992.0	59262.0
				PIII(M18)	49	49	100	92.7	100	5342.3	3989.1	7154.7	600.0	37234.0
				PIII(M24)	48	48	100	92.6	100	4112.1	3032.1	5576.8	557.0	31073.0
				PIII(M36)	49	49	100	92.7	100	3440.9	2566.1	4613.9	428.0	30440.0
				PIII(M48)	49	49	100	92.7	100	2753.3	2056.4	3686.5	183.0	15706.0
			S+	PRE	7	7	100	59.0	100	13.3	9.5	18.7	9.0	26.0
				PIII(M7)	7	7	100	59.0	100	17621.9	9057.5	34284.6	8602.0	53482.0
				PIII(M12)	7	7	100	59.0	100	7441.0	4508.7	12280.4	3755.0	17083.0
				PIII(M18)	7	7	100	59.0	100	5065.8	3441.4	7456.8	2757.0	9524.0
				PIII(M24)	7	7	100	59.0	100	4256.5	3030.9	5977.6	2567.0	8511.0
				PIII(M36)	7	7	100	59.0	100	3970.0	2878.4	5475.7	2120.0	5895.0
				PIII(M48)	7	7	100	59.0	100	3032.3	1775.5	5178.6	1565.0	8003.0
			Total	PRE	56	7	12.5	5.2	24.1	4.6	4.2	5.2	<8.0	26.0
				PIII(M7)	56	56	100	93.6	100	22054.4	17406.0	27944.1	3932.0	149951.0
				PIII(M12)	56	56	100	93.6	100	7828.9	5954.0	10294.2	992.0	59262.0
				PIII(M18)	56	56	100	93.6	100	5307.0	4103.7	6863.1	600.0	37234.0
				PIII(M24)	55	55	100	93.5	100	4130.2	3163.3	5392.7	557.0	31073.0

						≥ 8 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M36)	56	56	100	93.6	100	3503.0	2707.3	4532.5	428.0	30440.0
				PIII(M48)	56	56	100	93.6	100	2786.8	2149.9	3612.3	183.0	15706.0
		15_25	S-	PRE	80	0	0.0	0.0	4.5	4.0	4.0	4.0	<8.0	<8.0
				PIII(M7)	80	80	100	95.5	100	11837.1	9351.6	14983.3	1322.0	148276.0
				PIII(M12)	79	79	100	95.4	100	3930.5	3077.2	5020.4	182.0	81240.0
				PIII(M18)	79	79	100	95.4	100	2544.8	2011.6	3219.4	116.0	45075.0
				PIII(M24)	79	79	100	95.4	100	1989.0	1572.3	2516.0	112.0	35172.0
				PIII(M36)	80	80	100	95.5	100	1708.2	1358.9	2147.3	73.0	23603.0
				PIII(M48)	80	80	100	95.5	100	1419.6	1133.9	1777.2	71.0	17426.0
			S+	PRE	12	12	100	73.5	100	42.5	17.0	106.3	9.0	745.0
				PIII(M7)	12	12	100	73.5	100	9130.3	4151.9	20078.1	2482.0	99665.0
				PIII(M12)	12	12	100	73.5	100	4307.7	1965.3	9442.2	1156.0	51632.0
				PIII(M18)	12	12	100	73.5	100	3412.8	1558.7	7472.6	951.0	52061.0
				PIII(M24)	12	12	100	73.5	100	2643.7	1215.7	5749.2	812.0	37420.0
				PIII(M36)	12	12	100	73.5	100	2359.2	1078.5	5161.0	621.0	36109.0
				PIII(M48)	12	12	100	73.5	100	2112.0	974.0	4579.5	515.0	26218.0
			Total	PRE	92	12	13.0	6.9	21.7	5.4	4.5	6.6	<8.0	745.0
				PIII(M7)	92	92	100	96.1	100	11443.0	9148.7	14312.6	1322.0	148276.0
				PIII(M12)	91	91	100	96.0	100	3978.3	3160.1	5008.2	182.0	81240.0
				PIII(M18)	91	91	100	96.0	100	2645.2	2115.6	3307.5	116.0	52061.0
				PIII(M24)	91	91	100	96.0	100	2065.0	1652.2	2580.9	112.0	37420.0
				PIII(M36)	92	92	100	96.1	100	1781.7	1432.1	2216.7	73.0	36109.0
				PIII(M48)	92	92	100	96.1	100	1495.1	1205.3	1854.5	71.0	26218.0

V40_02 = HPV-16/18(40,40) AS04 0,2 m
V40_06 = HPV-16/18(40,40) AS04 0,6m
V20_06 = HPV-16/18(20,20) AS04 0,6 m
HPV = HPV-16/18(20,20) AS04 0,1,6m
S- = seronegative subjects (antibody concentration < 8 ELU/ML) prior to vaccination
S+ = seropositive subjects (antibody concentration ≥ 8 ELU/ML) prior to vaccination
GMT = geometric mean titers concentration calculated on all subjects
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with concentration equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = pre-vaccination
PII(M3) = Post Dose II, Month 3
PIII(M7) = Post Dose III, Month 7
PIII(M12) = Post Dose III, Month 12
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

Table 20 Number and percentage of subjects with an anti-HPV 18.VLP IGG concentration equal to or above the cut-off of 7 ELU/ML and GMTs in subjects aged 9-14 years and 15-25 years (Month 48 ATP Immunogenicity Cohort)

						≥ 7 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
HPV 18.VLP IGG	V40_02	9_14	S-	PRE	56	0	0.0	0.0	6.4	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	56	56	100	93.6	100	4957.6	3982.5	6171.5	562.0	33045.0
				PIII(M7)	56	56	100	93.6	100	1108.8	857.4	1433.9	69.0	7965.0
				PIII(M12)	56	56	100	93.6	100	584.6	442.9	771.5	35.0	5521.0
				PIII(M18)	55	55	100	93.5	100	485.9	371.7	635.3	50.0	3262.0
				PIII(M24)	55	55	100	93.5	100	419.0	318.1	551.9	37.0	3257.0
				PIII(M36)	55	55	100	93.5	100	409.4	307.6	544.7	29.0	6446.0
				PIII(M48)	56	56	100	93.6	100	344.8	260.1	457.3	31.0	5240.0
			S+	PRE	5	5	100	47.8	100	15.7	8.9	27.9	8.0	24.0
				PII(M3)	5	5	100	47.8	100	4361.8	1615.3	11778.3	2098.0	14980.0
				PIII(M7)	5	5	100	47.8	100	962.8	365.5	2536.5	286.0	2502.0
				PIII(M12)	5	5	100	47.8	100	458.8	134.5	1564.7	111.0	1205.0
				PIII(M18)	5	5	100	47.8	100	382.4	122.1	1197.9	115.0	1292.0
				PIII(M24)	5	5	100	47.8	100	429.6	116.9	1579.1	89.0	1189.0
				PIII(M36)	5	5	100	47.8	100	418.5	83.5	2097.5	86.0	2081.0
				PIII(M48)	5	5	100	47.8	100	359.4	67.0	1927.0	81.0	2353.0
			Total	PRE	61	5	8.2	2.7	18.1	4.0	3.5	4.4	<7.0	24.0
				PII(M3)	61	61	100	94.1	100	4905.9	3986.2	6037.7	562.0	33045.0
				PIII(M7)	61	61	100	94.1	100	1096.0	861.1	1395.0	69.0	7965.0
				PIII(M12)	61	61	100	94.1	100	573.1	440.6	745.3	35.0	5521.0
				PIII(M18)	60	60	100	94.0	100	476.3	369.7	613.6	50.0	3262.0
				PIII(M24)	60	60	100	94.0	100	419.8	323.2	545.4	37.0	3257.0
				PIII(M36)	60	60	100	94.0	100	410.1	311.4	540.1	29.0	6446.0
				PIII(M48)	61	61	100	94.1	100	346.0	263.2	454.8	31.0	5240.0
		15_25	S-	PRE	82	0	0.0	0.0	4.4	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	82	82	100	95.6	100	2965.0	2403.5	3657.7	148.0	22529.0
				PIII(M7)	82	82	100	95.6	100	632.7	515.0	777.4	73.0	4507.0
				PIII(M12)	82	82	100	95.6	100	356.9	285.9	445.7	25.0	2969.0
				PIII(M18)	81	81	100	95.5	100	289.2	230.9	362.2	15.0	2259.0
				PIII(M24)	78	78	100	95.4	100	245.0	194.7	308.2	12.0	1823.0
				PIII(M36)	80	80	100	95.5	100	234.1	183.7	298.3	10.0	2104.0
				PIII(M48)	82	82	100	95.6	100	208.9	163.5	267.0	9.0	1924.0
			S+	PRE	17	17	100	80.5	100	22.8	11.8	44.0	7.0	510.0
				PII(M3)	17	17	100	80.5	100	3178.7	1973.8	5119.1	671.0	33321.0
				PIII(M7)	17	17	100	80.5	100	931.0	546.3	1586.8	155.0	7467.0
				PIII(M12)	17	17	100	80.5	100	534.1	306.5	930.8	84.0	3415.0
				PIII(M18)	17	17	100	80.5	100	468.0	260.4	841.2	63.0	3091.0
				PIII(M24)	17	17	100	80.5	100	409.0	230.6	725.4	46.0	2332.0
				PIII(M36)	17	17	100	80.5	100	301.1	168.7	537.3	35.0	1826.0
				PIII(M48)	17	17	100	80.5	100	271.4	149.0	494.4	28.0	1700.0
			Total	PRE	99	17	17.2	10.3	26.1	4.8	4.1	5.8	<7.0	510.0
				PII(M3)	99	99	100	96.3	100	3000.7	2484.5	3624.0	148.0	33321.0
				PIII(M7)	99	99	100	96.3	100	676.1	558.2	818.9	73.0	7467.0
				PIII(M12)	99	99	100	96.3	100	382.5	311.6	469.6	25.0	3415.0
				PIII(M18)	98	98	100	96.3	100	314.4	254.7	388.1	15.0	3091.0

						≥ 7 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M24)	95	95	100	96.2	100	268.5	216.8	332.5	12.0	2332.0
				PIII(M36)	97	97	100	96.3	100	244.7	196.2	305.0	10.0	2104.0
				PIII(M48)	99	99	100	96.3	100	218.5	174.7	273.4	9.0	1924.0
	V40_06	9_14	S-	PRE	51	0	0.0	0.0	7.0	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	51	51	100	93.0	100	270.4	206.8	353.6	46.0	3159.0
				PIII(M7)	51	51	100	93.0	100	8863.3	7099.7	11065.2	1202.0	60059.0
				PIII(M12)	51	51	100	93.0	100	2193.3	1690.9	2845.0	361.0	20569.0
				PIII(M18)	51	51	100	93.0	100	1254.7	959.7	1640.4	193.0	11555.0
				PIII(M24)	50	50	100	92.9	100	957.7	727.0	1261.6	184.0	6809.0
				PIII(M36)	51	51	100	93.0	100	765.3	585.0	1001.1	124.0	4814.0
				PIII(M48)	51	51	100	93.0	100	683.5	518.3	901.4	119.0	7909.0
			Total	PRE	51	0	0.0	0.0	7.0	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	51	51	100	93.0	100	270.4	206.8	353.6	46.0	3159.0
				PIII(M7)	51	51	100	93.0	100	8863.3	7099.7	11065.2	1202.0	60059.0
				PIII(M12)	51	51	100	93.0	100	2193.3	1690.9	2845.0	361.0	20569.0
				PIII(M18)	51	51	100	93.0	100	1254.7	959.7	1640.4	193.0	11555.0
				PIII(M24)	50	50	100	92.9	100	957.7	727.0	1261.6	184.0	6809.0
				PIII(M36)	51	51	100	93.0	100	765.3	585.0	1001.1	124.0	4814.0
				PIII(M48)	51	51	100	93.0	100	683.5	518.3	901.4	119.0	7909.0
		15_25	S-	PRE	88	0	0.0	0.0	4.1	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	88	88	100	95.9	100	199.3	159.0	249.9	13.0	7952.0
				PIII(M7)	88	88	100	95.9	100	5804.1	4815.0	6996.4	412.0	91976.0
				PIII(M12)	87	87	100	95.8	100	1715.3	1385.4	2123.9	190.0	34743.0
				PIII(M18)	86	86	100	95.8	100	997.3	793.4	1253.7	102.0	19845.0
				PIII(M24)	86	86	100	95.8	100	789.2	633.2	983.8	73.0	15066.0
				PIII(M36)	86	86	100	95.8	100	694.2	555.6	867.4	50.0	15050.0
				PIII(M48)	88	88	100	95.9	100	567.3	456.6	704.9	45.0	10456.0
			S+	PRE	14	14	100	76.8	100	24.8	11.8	52.1	8.0	387.0
				PII(M3)	14	14	100	76.8	100	1065.9	450.2	2523.4	152.0	23563.0
				PIII(M7)	14	14	100	76.8	100	6768.3	3639.8	12585.8	619.0	25115.0
				PIII(M12)	14	14	100	76.8	100	2571.7	1335.8	4951.1	240.0	9748.0
				PIII(M18)	13	13	100	75.3	100	1560.1	760.8	3199.2	218.0	7798.0
				PIII(M24)	13	13	100	75.3	100	1357.2	674.4	2731.4	155.0	8456.0
				PIII(M36)	14	14	100	76.8	100	1009.4	483.8	2106.1	116.0	6960.0
				PIII(M48)	14	14	100	76.8	100	848.2	414.2	1737.3	95.0	6170.0
			Total	PRE	102	14	13.7	7.7	22.0	4.6	3.9	5.4	<7.0	387.0
				PII(M3)	102	102	100	96.4	100	250.9	195.6	321.8	13.0	23563.0
				PIII(M7)	102	102	100	96.4	100	5927.8	4961.3	7082.6	412.0	91976.0
				PIII(M12)	101	101	100	96.4	100	1814.4	1481.9	2221.4	190.0	34743.0
				PIII(M18)	99	99	100	96.3	100	1057.7	851.4	1314.0	102.0	19845.0
				PIII(M24)	99	99	100	96.3	100	847.5	686.6	1046.0	73.0	15066.0
				PIII(M36)	100	100	100	96.4	100	731.6	591.0	905.6	50.0	15050.0
				PIII(M48)	102	102	100	96.4	100	599.5	486.9	738.2	45.0	10456.0
	V20_06	9_14	S-	PRE	52	0	0.0	0.0	6.8	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	52	52	100	93.2	100	211.8	156.9	285.8	41.0	5333.0
				PIII(M7)	52	52	100	93.2	100	5778.5	4786.5	6976.1	1094.0	36047.0
				PIII(M12)	52	52	100	93.2	100	1624.3	1284.7	2053.6	178.0	11420.0
				PIII(M18)	52	52	100	93.2	100	936.6	736.8	1190.7	95.0	5228.0
				PIII(M24)	51	51	100	93.0	100	727.7	570.8	927.6	92.0	4440.0
				PIII(M36)	50	50	100	92.9	100	646.0	500.3	834.0	103.0	5844.0

						≥ 7 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M48)	52	52	100	93.2	100	542.9	426.5	691.0	103.0	2928.0
			S+	PRE	3	3	100	29.2	100	8.0	5.8	10.9	7.0	9.0
				PII(M3)	3	3	100	29.2	100	207.3	76.6	561.3	140.0	312.0
				PIII(M7)	3	3	100	29.2	100	8010.4	2256.9	28431.7	4474.0	11551.0
				PIII(M12)	3	3	100	29.2	100	2115.0	502.1	8908.4	1102.0	3329.0
				PIII(M18)	3	3	100	29.2	100	1075.2	277.2	4169.8	636.0	1890.0
				PIII(M24)	3	3	100	29.2	100	909.5	327.0	2529.1	678.0	1456.0
				PIII(M36)	3	3	100	29.2	100	686.4	188.7	2497.3	457.0	1233.0
				PIII(M48)	3	3	100	29.2	100	597.2	314.0	1135.5	482.0	796.0
			Total	PRE	55	3	5.5	1.1	15.1	3.7	3.5	3.9	<7.0	9.0
				PII(M3)	55	55	100	93.5	100	211.5	159.3	280.9	41.0	5333.0
				PIII(M7)	55	55	100	93.5	100	5882.4	4909.2	7048.4	1094.0	36047.0
				PIII(M12)	55	55	100	93.5	100	1647.8	1317.2	2061.5	178.0	11420.0
				PIII(M18)	55	55	100	93.5	100	943.7	751.0	1185.9	95.0	5228.0
				PIII(M24)	54	54	100	93.4	100	736.7	585.2	927.5	92.0	4440.0
				PIII(M36)	53	53	100	93.3	100	648.2	508.8	825.9	103.0	5844.0
				PIII(M48)	55	55	100	93.5	100	545.7	434.4	685.6	103.0	2928.0
		15_25	S-	PRE	83	0	0.0	0.0	4.3	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	83	83	100	95.7	100	168.1	130.5	216.5	16.0	4646.0
				PIII(M7)	83	83	100	95.7	100	5013.3	4168.8	6028.8	551.0	34562.0
				PIII(M12)	83	83	100	95.7	100	1417.3	1137.6	1765.9	99.0	10163.0
				PIII(M18)	83	83	100	95.7	100	895.6	715.9	1120.5	45.0	5847.0
				PIII(M24)	81	81	100	95.5	100	711.3	569.5	888.4	43.0	4669.0
				PIII(M36)	82	82	100	95.6	100	618.8	491.1	779.6	30.0	3297.0
				PIII(M48)	83	83	100	95.7	100	521.4	415.4	654.4	33.0	3668.0
			S+	PRE	19	19	100	82.4	100	24.0	14.5	39.8	7.0	141.0
				PII(M3)	19	19	100	82.4	100	461.9	249.5	855.0	98.0	4199.0
				PIII(M7)	19	19	100	82.4	100	4425.1	3125.2	6265.8	1851.0	18651.0
				PIII(M12)	19	19	100	82.4	100	1379.9	959.8	1983.7	499.0	7031.0
				PIII(M18)	18	18	100	81.5	100	845.3	580.1	1232.0	258.0	3527.0
				PIII(M24)	19	19	100	82.4	100	657.3	473.1	913.1	209.0	2956.0
				PIII(M36)	18	18	100	81.5	100	546.7	380.8	784.8	152.0	2292.0
				PIII(M48)	19	19	100	82.4	100	426.0	308.2	588.9	155.0	1568.0
			Total	PRE	102	19	18.6	11.6	27.6	5.0	4.2	5.9	<7.0	141.0
				PII(M3)	102	102	100	96.4	100	202.9	159.0	258.9	16.0	4646.0
				PIII(M7)	102	102	100	96.4	100	4898.1	4168.3	5755.6	551.0	34562.0
				PIII(M12)	102	102	100	96.4	100	1410.3	1167.6	1703.4	99.0	10163.0
				PIII(M18)	101	101	100	96.4	100	886.4	730.5	1075.7	45.0	5847.0
				PIII(M24)	100	100	100	96.4	100	700.7	580.3	846.0	43.0	4669.0
				PIII(M36)	100	100	100	96.4	100	605.1	496.3	737.8	30.0	3297.0
				PIII(M48)	102	102	100	96.4	100	502.1	414.0	609.1	33.0	3668.0
	HPV	9_14	S-	PRE	50	0	0.0	0.0	7.1	3.5	3.5	3.5	<7.0	<7.0
				PIII(M7)	50	50	100	92.9	100	7685.5	6024.5	9804.6	1680.0	37491.0
				PIII(M12)	50	50	100	92.9	100	2562.4	1877.7	3497.0	339.0	19004.0
				PIII(M18)	50	50	100	92.9	100	1617.6	1213.5	2156.3	247.0	8773.0
				PIII(M24)	49	49	100	92.7	100	1323.9	985.1	1779.1	187.0	8369.0
				PIII(M36)	50	50	100	92.9	100	1166.6	879.0	1548.4	139.0	8194.0
				PIII(M48)	50	50	100	92.9	100	954.7	716.9	1271.4	101.0	6125.0
			S+	PRE	6	6	100	54.1	100	15.9	7.6	33.6	8.0	43.0
				PIII(M7)	6	6	100	54.1	100	6112.6	3530.0	10584.4	2806.0	11503.0
				PIII(M12)	6	6	100	54.1	100	2149.9	1183.2	3906.5	687.0	3126.0

						≥ 7 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M18)	6	6	100	54.1	100	1519.1	787.4	2930.4	466.0	2997.0
				PIII(M24)	6	6	100	54.1	100	1206.3	635.7	2289.1	420.0	2477.0
				PIII(M36)	6	6	100	54.1	100	1207.2	641.8	2270.5	475.0	2582.0
				PIII(M48)	6	6	100	54.1	100	864.1	440.1	1696.5	302.0	1976.0
			Total	PRE	56	6	10.7	4.0	21.9	4.1	3.6	4.7	<7.0	43.0
				PIII(M7)	56	56	100	93.6	100	7499.2	6009.3	9358.6	1680.0	37491.0
				PIII(M12)	56	56	100	93.6	100	2514.7	1899.2	3329.7	339.0	19004.0
				PIII(M18)	56	56	100	93.6	100	1606.7	1238.1	2085.2	247.0	8773.0
				PIII(M24)	55	55	100	93.5	100	1310.5	1003.3	1711.8	187.0	8369.0
				PIII(M36)	56	56	100	93.6	100	1170.9	906.0	1513.2	139.0	8194.0
				PIII(M48)	56	56	100	93.6	100	944.6	728.2	1225.2	101.0	6125.0
		15_25	S-	PRE	79	0	0.0	0.0	4.6	3.5	3.5	3.5	<7.0	<7.0
				PIII(M7)	79	79	100	95.4	100	4637.8	3775.6	5696.8	1030.0	69885.0
				PIII(M12)	78	78	100	95.4	100	1548.3	1225.2	1956.6	167.0	26768.0
				PIII(M18)	78	78	100	95.4	100	1023.0	804.1	1301.4	65.0	19963.0
				PIII(M24)	78	78	100	95.4	100	817.8	641.8	1042.0	39.0	13295.0
				PIII(M36)	79	79	100	95.4	100	735.1	573.9	941.7	25.0	9702.0
				PIII(M48)	79	79	100	95.4	100	604.5	475.9	768.0	18.0	7320.0
			S+	PRE	13	13	100	75.3	100	14.6	8.9	24.0	7.0	130.0
				PIII(M7)	13	13	100	75.3	100	4147.0	1971.4	8723.3	926.0	81284.0
				PIII(M12)	13	13	100	75.3	100	1560.9	693.3	3514.2	363.0	47033.0
				PIII(M18)	13	13	100	75.3	100	1122.9	511.6	2464.4	197.0	29745.0
				PIII(M24)	13	13	100	75.3	100	842.4	373.8	1898.8	176.0	24394.0
				PIII(M36)	13	13	100	75.3	100	786.1	348.8	1771.6	206.0	24703.0
				PIII(M48)	13	13	100	75.3	100	680.4	296.0	1564.3	168.0	21133.0
			Total	PRE	92	13	14.1	7.7	23.0	4.3	3.8	4.8	<7.0	130.0
				PIII(M7)	92	92	100	96.1	100	4565.0	3741.0	5570.5	926.0	81284.0
				PIII(M12)	91	91	100	96.0	100	1550.1	1238.3	1940.3	167.0	47033.0
				PIII(M18)	91	91	100	96.0	100	1036.7	825.1	1302.5	65.0	29745.0
				PIII(M24)	91	91	100	96.0	100	821.3	652.0	1034.6	39.0	24394.0
				PIII(M36)	92	92	100	96.1	100	742.1	586.8	938.6	25.0	24703.0
				PIII(M48)	92	92	100	96.1	100	614.7	488.6	773.4	18.0	21133.0

V40_02 = HPV-16/18(40,40) AS04 0,2 m
V40_06 = HPV-16/18(40,40) AS04 0,6m
V20_06 = HPV-16/18(20,20) AS04 0,6 m
HPV = HPV-16/18(20,20) AS04 0,1,6m
S- = seronegative subjects (antibody concentration < 7 ELU/ML) prior to vaccination
S+ = seropositive subjects (antibody concentration ≥ 7 ELU/ML) prior to vaccination
GMT = geometric mean titers concentration calculated on all subjects
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with concentration equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = pre-vaccination
PII(M3) = Post Dose II, Month 3
PIII(M7) = Post Dose III, Month 7
PIII(M12) = Post Dose III, Month 12
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

Table 21 Number and percentage of subjects with an anti-HPV 16.VLP IGG concentration equal to or above the cut-off of 8 ELU/ML and GMTs by age stratum (Month 48 ATP Immunogenicity Cohort)

						≥ 8 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
HPV 16.VLP IGG	V40_02	9_14y	S-	PRE	61	0	0.0	0.0	5.9	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	61	61	100	94.1	100	7233.1	5876.8	8902.6	966.0	45534.0
				PIII(M7)	61	61	100	94.1	100	2011.9	1578.3	2564.7	208.0	26271.0
				PIII(M12)	61	61	100	94.1	100	1434.5	1114.6	1846.3	143.0	17994.0
				PIII(M18)	60	60	100	94.0	100	1385.7	1064.0	1804.7	138.0	11507.0
				PIII(M24)	60	60	100	94.0	100	1158.6	898.8	1493.6	124.0	9500.0
				PIII(M36)	60	60	100	94.0	100	996.3	777.5	1276.6	117.0	10491.0
				PIII(M48)	61	61	100	94.1	100	908.6	721.4	1144.3	100.0	6475.0
			Total	PRE	61	0	0.0	0.0	5.9	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	61	61	100	94.1	100	7233.1	5876.8	8902.6	966.0	45534.0
				PIII(M7)	61	61	100	94.1	100	2011.9	1578.3	2564.7	208.0	26271.0
				PIII(M12)	61	61	100	94.1	100	1434.5	1114.6	1846.3	143.0	17994.0
				PIII(M18)	60	60	100	94.0	100	1385.7	1064.0	1804.7	138.0	11507.0
				PIII(M24)	60	60	100	94.0	100	1158.6	898.8	1493.6	124.0	9500.0
				PIII(M36)	60	60	100	94.0	100	996.3	777.5	1276.6	117.0	10491.0
				PIII(M48)	61	61	100	94.1	100	908.6	721.4	1144.3	100.0	6475.0
		15_19y	S-	PRE	51	0	0.0	0.0	7.0	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	51	51	100	93.0	100	5105.1	4040.6	6450.0	233.0	19508.0
				PIII(M7)	51	51	100	93.0	100	1111.1	871.9	1416.0	148.0	6111.0
				PIII(M12)	51	51	100	93.0	100	779.1	612.5	991.1	123.0	4466.0
				PIII(M18)	51	51	100	93.0	100	708.7	541.8	926.9	96.0	4620.0
				PIII(M24)	49	49	100	92.7	100	621.9	488.0	792.6	100.0	2516.0
				PIII(M36)	50	50	100	92.9	100	539.4	417.1	697.4	71.0	2219.0
				PIII(M48)	51	51	100	93.0	100	521.7	400.7	679.3	36.0	1994.0
			S+	PRE	3	3	100	29.2	100	30.7	12.1	77.5	20.0	40.0
				PII(M3)	3	3	100	29.2	100	5788.0	2330.9	14372.6	3811.0	7540.0
				PIII(M7)	3	3	100	29.2	100	2093.3	1237.7	3540.2	1698.0	2592.0
				PIII(M12)	3	3	100	29.2	100	1225.4	535.1	2806.1	893.0	1736.0
				PIII(M18)	3	3	100	29.2	100	1382.4	601.6	3176.1	1006.0	1961.0
				PIII(M24)	3	3	100	29.2	100	891.2	583.3	1361.8	735.0	1017.0
				PIII(M36)	3	3	100	29.2	100	862.1	447.2	1661.8	677.0	1143.0
				PIII(M48)	3	3	100	29.2	100	760.3	236.3	2446.5	442.0	1024.0
			Total	PRE	54	3	5.6	1.2	15.4	4.5	3.9	5.1	<8.0	40.0
				PII(M3)	54	54	100	93.4	100	5140.8	4119.8	6414.9	233.0	19508.0
				PIII(M7)	54	54	100	93.4	100	1150.9	912.3	1451.8	148.0	6111.0
				PIII(M12)	54	54	100	93.4	100	799.0	635.3	1004.9	123.0	4466.0
				PIII(M18)	54	54	100	93.4	100	735.5	568.7	951.2	96.0	4620.0
				PIII(M24)	52	52	100	93.2	100	635.0	504.8	798.8	100.0	2516.0
				PIII(M36)	53	53	100	93.3	100	553.9	433.9	707.1	71.0	2219.0
				PIII(M48)	54	54	100	93.4	100	532.8	414.5	684.8	36.0	1994.0
		20_25y	S-	PRE	37	0	0.0	0.0	9.5	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	37	37	100	90.5	100	4637.4	3527.3	6096.9	668.0	22930.0
				PIII(M7)	37	37	100	90.5	100	1141.7	839.4	1552.7	80.0	5616.0
				PIII(M12)	37	37	100	90.5	100	792.6	569.8	1102.3	53.0	3727.0
				PIII(M18)	37	37	100	90.5	100	717.8	501.9	1026.5	32.0	5415.0
				PIII(M24)	37	37	100	90.5	100	601.6	426.4	848.9	24.0	2959.0

						≥ 8 ELU/ML				GMT				
							95% CI				95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M36)	37	37	100	90.5	100	527.3	379.4	732.9	29.0	2701.0
				PIII(M48)	37	37	100	90.5	100	489.2	341.3	701.2	21.0	3403.0
			S+	PRE	8	8	100	63.1	100	35.8	11.2	114.4	9.0	413.0
				PII(M3)	8	8	100	63.1	100	4994.8	2163.1	11533.4	1744.0	20636.0
				PIII(M7)	8	8	100	63.1	100	1824.2	699.2	4759.1	521.0	11429.0
				PIII(M12)	8	8	100	63.1	100	1482.6	615.4	3571.8	338.0	7667.0
				PIII(M18)	7	7	100	59.0	100	1070.0	385.9	2966.3	281.0	5156.0
				PIII(M24)	6	6	100	54.1	100	792.5	201.4	3119.2	184.0	6264.0
				PIII(M36)	7	7	100	59.0	100	689.9	208.4	2284.4	120.0	5741.0
				PIII(M48)	8	8	100	63.1	100	709.7	258.3	1949.8	101.0	4785.0
			Total	PRE	45	8	17.8	8.0	32.1	5.9	4.4	8.0	<8.0	413.0
				PII(M3)	45	45	100	92.1	100	4699.0	3647.3	6054.0	668.0	22930.0
				PIII(M7)	45	45	100	92.1	100	1240.9	927.6	1660.0	80.0	11429.0
				PIII(M12)	45	45	100	92.1	100	885.9	652.5	1202.7	53.0	7667.0
				PIII(M18)	44	44	100	92.0	100	764.9	551.7	1060.5	32.0	5415.0
				PIII(M24)	43	43	100	91.8	100	625.2	451.0	866.7	24.0	6264.0
				PIII(M36)	44	44	100	92.0	100	550.4	402.4	752.6	29.0	5741.0
				PIII(M48)	45	45	100	92.1	100	522.6	375.7	727.0	21.0	4785.0
	V40_06	9_14y	S-	PRE	49	0	0.0	0.0	7.3	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	49	49	100	92.7	100	374.2	281.1	498.2	43.0	7324.0
				PIII(M7)	49	49	100	92.7	100	17103.0	13939.1	20985.1	2713.0	57135.0
				PIII(M12)	49	49	100	92.7	100	4465.5	3538.0	5636.2	877.0	30300.0
				PIII(M18)	49	49	100	92.7	100	2931.7	2338.4	3675.4	600.0	12570.0
				PIII(M24)	48	48	100	92.6	100	2153.3	1711.2	2709.5	341.0	9840.0
				PIII(M36)	49	49	100	92.7	100	1743.3	1397.8	2174.2	239.0	8472.0
				PIII(M48)	49	49	100	92.7	100	1552.6	1218.5	1978.3	202.0	11546.0
			Total	PRE	49	0	0.0	0.0	7.3	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	49	49	100	92.7	100	374.2	281.1	498.2	43.0	7324.0
				PIII(M7)	49	49	100	92.7	100	17103.0	13939.1	20985.1	2713.0	57135.0
				PIII(M12)	49	49	100	92.7	100	4465.5	3538.0	5636.2	877.0	30300.0
				PIII(M18)	49	49	100	92.7	100	2931.7	2338.4	3675.4	600.0	12570.0
				PIII(M24)	48	48	100	92.6	100	2153.3	1711.2	2709.5	341.0	9840.0
				PIII(M36)	49	49	100	92.7	100	1743.3	1397.8	2174.2	239.0	8472.0
				PIII(M48)	49	49	100	92.7	100	1552.6	1218.5	1978.3	202.0	11546.0
		15_19y	S-	PRE	46	0	0.0	0.0	7.7	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	46	46	100	92.3	100	382.7	281.1	521.0	61.0	5303.0
				PIII(M7)	46	46	100	92.3	100	12073.4	9552.6	15259.4	1426.0	38586.0
				PIII(M12)	46	46	100	92.3	100	3942.7	3178.8	4890.3	389.0	13772.0
				PIII(M18)	45	45	100	92.1	100	2490.0	1984.2	3124.6	516.0	11355.0
				PIII(M24)	45	45	100	92.1	100	1977.6	1577.4	2479.3	352.0	8639.0
				PIII(M36)	46	46	100	92.3	100	1626.7	1295.5	2042.5	283.0	7742.0
				PIII(M48)	46	46	100	92.3	100	1293.7	1036.8	1614.1	282.0	5087.0
			S+	PRE	5	5	100	47.8	100	65.2	7.3	581.6	12.0	594.0
				PII(M3)	5	5	100	47.8	100	1101.1	192.0	6315.7	173.0	6052.0
				PIII(M7)	5	5	100	47.8	100	11712.1	5387.8	25460.0	6935.0	33723.0
				PIII(M12)	5	5	100	47.8	100	3143.6	868.4	11380.1	697.0	11023.0
				PIII(M18)	5	5	100	47.8	100	2186.6	429.3	11138.4	284.0	8045.0
				PIII(M24)	5	5	100	47.8	100	1986.1	460.8	8560.5	357.0	6774.0
				PIII(M36)	5	5	100	47.8	100	1419.7	241.5	8345.8	157.0	7224.0
				PIII(M48)	5	5	100	47.8	100	1221.6	198.8	7507.2	147.0	6467.0
			Total	PRE	51	5	9.8	3.3	21.4	5.3	4.0	6.9	<8.0	594.0

						≥ 8 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PII(M3)	51	51	100	93.0	100	424.5	310.7	579.9	61.0	6052.0
				PIII(M7)	51	51	100	93.0	100	12037.5	9696.7	14943.3	1426.0	38586.0
				PIII(M12)	51	51	100	93.0	100	3856.1	3122.0	4763.0	389.0	13772.0
				PIII(M18)	50	50	100	92.9	100	2457.8	1952.9	3093.3	284.0	11355.0
				PIII(M24)	50	50	100	92.9	100	1978.4	1581.3	2475.3	352.0	8639.0
				PIII(M36)	51	51	100	93.0	100	1605.1	1270.0	2028.7	157.0	7742.0
				PIII(M48)	51	51	100	93.0	100	1286.4	1021.7	1619.7	147.0	6467.0
		20_25y	S-	PRE	35	0	0.0	0.0	10.0	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	35	35	100	90.0	100	287.8	200.4	413.4	45.0	3769.0
				PIII(M7)	35	35	100	90.0	100	9103.0	6909.6	11992.6	1211.0	48115.0
				PIII(M12)	34	34	100	89.7	100	2421.9	1758.7	3335.0	109.0	20072.0
				PIII(M18)	33	33	100	89.4	100	1772.8	1272.1	2470.6	107.0	15410.0
				PIII(M24)	33	33	100	89.4	100	1365.4	999.3	1865.5	138.0	11571.0
				PIII(M36)	33	33	100	89.4	100	1187.8	904.2	1560.5	288.0	7105.0
				PIII(M48)	35	35	100	90.0	100	1006.1	770.2	1314.2	178.0	5176.0
			S+	PRE	16	16	100	79.4	100	61.9	31.5	121.7	10.0	345.0
				PII(M3)	16	16	100	79.4	100	1700.6	795.0	3637.7	139.0	11769.0
				PIII(M7)	16	16	100	79.4	100	5823.5	3714.1	9130.9	1534.0	29466.0
				PIII(M12)	16	16	100	79.4	100	2714.7	1804.5	4083.9	499.0	8153.0
				PIII(M18)	16	16	100	79.4	100	1919.3	1230.5	2993.6	344.0	5765.0
				PIII(M24)	16	16	100	79.4	100	1470.2	943.6	2290.6	288.0	5058.0
				PIII(M36)	16	16	100	79.4	100	1197.0	805.7	1778.3	234.0	2968.0
				PIII(M48)	16	16	100	79.4	100	1026.9	720.3	1463.8	249.0	2308.0
			Total	PRE	51	16	31.4	19.1	45.9	9.4	6.3	14.2	<8.0	345.0
				PII(M3)	51	51	100	93.0	100	502.5	335.6	752.4	45.0	11769.0
				PIII(M7)	51	51	100	93.0	100	7912.6	6258.2	10004.4	1211.0	48115.0
				PIII(M12)	50	50	100	92.9	100	2512.0	1964.2	3212.4	109.0	20072.0
				PIII(M18)	49	49	100	92.7	100	1819.4	1406.5	2353.5	107.0	15410.0
				PIII(M24)	49	49	100	92.7	100	1398.7	1093.6	1789.0	138.0	11571.0
				PIII(M36)	49	49	100	92.7	100	1190.8	959.1	1478.4	234.0	7105.0
				PIII(M48)	51	51	100	93.0	100	1012.6	822.9	1246.0	178.0	5176.0
	V20_06	9_14y	S-	PRE	53	0	0.0	0.0	6.7	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	53	53	100	93.3	100	274.0	211.8	354.5	73.0	6037.0
				PIII(M7)	53	53	100	93.3	100	12008.8	9732.2	14817.9	2687.0	60582.0
				PIII(M12)	53	53	100	93.3	100	3542.6	2932.6	4279.5	737.0	21151.0
				PIII(M18)	53	53	100	93.3	100	2351.2	1926.8	2869.0	529.0	10395.0
				PIII(M24)	52	52	100	93.2	100	1813.2	1489.3	2207.7	452.0	7302.0
				PIII(M36)	51	51	100	93.0	100	1530.8	1246.5	1880.0	356.0	7249.0
				PIII(M48)	53	53	100	93.3	100	1319.8	1084.1	1606.7	360.0	7307.0
			S+	PRE	2	2	100	15.8	100	10.8	1.0	111.9	9.0	13.0
				PII(M3)	2	2	100	15.8	100	216.6	16.7	2812.8	177.0	265.0
				PIII(M7)	2	2	100	15.8	100	10464.9	271.6	403258.3	7851.0	13949.0
				PIII(M12)	2	2	100	15.8	100	2833.5	246.4	32584.4	2338.0	3434.0
				PIII(M18)	2	2	100	15.8	100	2002.8	878.4	4566.4	1877.0	2137.0
				PIII(M24)	2	2	100	15.8	100	1021.0	188.9	5519.7	894.0	1166.0
				PIII(M36)	2	2	100	15.8	100	810.1	71.2	9219.5	669.0	981.0
				PIII(M48)	2	2	100	15.8	100	580.2	395.5	851.2	563.0	598.0
			Total	PRE	55	2	3.6	0.4	12.5	4.1	3.9	4.4	<8.0	13.0
				PII(M3)	55	55	100	93.5	100	271.7	211.9	348.2	73.0	6037.0
				PIII(M7)	55	55	100	93.5	100	11948.9	9753.8	14637.9	2687.0	60582.0
				PIII(M12)	55	55	100	93.5	100	3513.9	2927.7	4217.5	737.0	21151.0

						≥ 8 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M18)	55	55	100	93.5	100	2337.5	1929.6	2831.7	529.0	10395.0
				PIII(M24)	54	54	100	93.4	100	1775.1	1465.3	2150.3	452.0	7302.0
				PIII(M36)	53	53	100	93.3	100	1494.5	1222.8	1826.5	356.0	7249.0
				PIII(M48)	55	55	100	93.5	100	1280.9	1055.1	1555.0	360.0	7307.0
		15_19y	S-	PRE	48	0	0.0	0.0	7.4	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	48	48	100	92.6	100	284.3	202.6	398.9	28.0	7463.0
				PIII(M7)	48	48	100	92.6	100	8427.6	6604.8	10753.5	1436.0	47872.0
				PIII(M12)	48	48	100	92.6	100	2645.2	2106.5	3321.6	377.0	13560.0
				PIII(M18)	47	47	100	92.5	100	1903.5	1511.7	2396.8	246.0	12109.0
				PIII(M24)	47	47	100	92.5	100	1455.9	1179.5	1797.0	256.0	7638.0
				PIII(M36)	48	48	100	92.6	100	1239.5	1013.6	1515.8	221.0	5658.0
				PIII(M48)	48	48	100	92.6	100	1090.3	886.3	1341.3	262.0	6368.0
			S+	PRE	4	4	100	39.8	100	41.4	3.8	456.2	11.0	314.0
				PII(M3)	4	4	100	39.8	100	946.3	132.6	6750.9	377.0	5330.0
				PIII(M7)	4	4	100	39.8	100	5052.6	1510.7	16898.3	2182.0	10884.0
				PIII(M12)	4	4	100	39.8	100	2008.4	703.7	5731.7	1061.0	4980.0
				PIII(M18)	4	4	100	39.8	100	1332.9	556.8	3190.8	741.0	2686.0
				PIII(M24)	4	4	100	39.8	100	1007.8	444.3	2286.4	682.0	2089.0
				PIII(M36)	4	4	100	39.8	100	792.0	370.1	1694.9	454.0	1302.0
				PIII(M48)	4	4	100	39.8	100	780.5	425.4	1432.1	558.0	1089.0
			Total	PRE	52	4	7.7	2.1	18.5	4.8	3.9	5.9	<8.0	314.0
				PII(M3)	52	52	100	93.2	100	311.8	223.1	435.9	28.0	7463.0
				PIII(M7)	52	52	100	93.2	100	8102.4	6416.6	10231.1	1436.0	47872.0
				PIII(M12)	52	52	100	93.2	100	2589.7	2088.2	3211.7	377.0	13560.0
				PIII(M18)	51	51	100	93.0	100	1851.0	1490.3	2299.1	246.0	12109.0
				PIII(M24)	51	51	100	93.0	100	1414.5	1159.6	1725.3	256.0	7638.0
				PIII(M36)	52	52	100	93.2	100	1197.5	989.3	1449.5	221.0	5658.0
				PIII(M48)	52	52	100	93.2	100	1062.7	875.2	1290.2	262.0	6368.0
		20_25y	S-	PRE	38	0	0.0	0.0	9.3	4.0	4.0	4.0	<8.0	<8.0
				PII(M3)	38	38	100	90.7	100	188.9	132.5	269.3	25.0	1396.0
				PIII(M7)	38	38	100	90.7	100	5717.7	4311.0	7583.4	973.0	26064.0
				PIII(M12)	38	38	100	90.7	100	1652.6	1215.5	2247.0	290.0	12488.0
				PIII(M18)	38	38	100	90.7	100	1060.6	775.3	1450.9	159.0	7017.0
				PIII(M24)	37	37	100	90.5	100	820.6	600.3	1121.6	149.0	5366.0
				PIII(M36)	37	37	100	90.5	100	631.3	469.8	848.3	88.0	4054.0
				PIII(M48)	38	38	100	90.7	100	541.6	403.9	726.1	85.0	3181.0
			S+	PRE	12	12	100	73.5	100	50.9	27.2	95.3	11.0	337.0
				PII(M3)	12	12	100	73.5	100	2273.8	1262.9	4093.9	559.0	9225.0
				PIII(M7)	12	12	100	73.5	100	4487.3	2769.5	7270.7	1479.0	26064.0
				PIII(M12)	12	12	100	73.5	100	2365.1	1408.3	3971.8	970.0	12549.0
				PIII(M18)	12	12	100	73.5	100	1622.0	912.4	2883.3	628.0	6867.0
				PIII(M24)	12	12	100	73.5	100	1305.5	697.4	2444.0	384.0	7343.0
				PIII(M36)	11	11	100	71.5	100	1101.2	574.3	2111.6	360.0	5553.0
				PIII(M48)	12	12	100	73.5	100	924.3	505.0	1691.7	334.0	4949.0
			Total	PRE	50	12	24.0	13.1	38.2	7.4	5.2	10.3	<8.0	337.0
				PII(M3)	50	50	100	92.9	100	343.2	224.7	524.3	25.0	9225.0
				PIII(M7)	50	50	100	92.9	100	5394.6	4254.6	6840.2	973.0	26064.0
				PIII(M12)	50	50	100	92.9	100	1801.1	1389.6	2334.4	290.0	12549.0
				PIII(M18)	50	50	100	92.9	100	1174.4	896.4	1538.7	159.0	7017.0
				PIII(M24)	49	49	100	92.7	100	919.4	697.7	1211.5	149.0	7343.0
				PIII(M36)	48	48	100	92.6	100	717.1	548.1	938.3	88.0	5553.0

						≥ 8 ELU/ML				GMT				
							95% CI				95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M48)	50	50	100	92.9	100	615.7	473.3	801.0	85.0	4949.0
	HPV	9_14y	S-	PRE	49	0	0.0	0.0	7.3	4.0	4.0	4.0	<8.0	<8.0
				PIII(M7)	49	49	100	92.7	100	22772.7	17551.7	29546.9	3932.0	149951.0
				PIII(M12)	49	49	100	92.7	100	7886.0	5787.4	10745.4	992.0	59262.0
				PIII(M18)	49	49	100	92.7	100	5342.3	3989.1	7154.7	600.0	37234.0
				PIII(M24)	48	48	100	92.6	100	4112.1	3032.1	5576.8	557.0	31073.0
				PIII(M36)	49	49	100	92.7	100	3440.9	2566.1	4613.9	428.0	30440.0
				PIII(M48)	49	49	100	92.7	100	2753.3	2056.4	3686.5	183.0	15706.0
			S+	PRE	7	7	100	59.0	100	13.3	9.5	18.7	9.0	26.0
				PIII(M7)	7	7	100	59.0	100	17621.9	9057.5	34284.6	8602.0	53482.0
				PIII(M12)	7	7	100	59.0	100	7441.0	4508.7	12280.4	3755.0	17083.0
				PIII(M18)	7	7	100	59.0	100	5065.8	3441.4	7456.8	2757.0	9524.0
				PIII(M24)	7	7	100	59.0	100	4256.5	3030.9	5977.6	2567.0	8511.0
				PIII(M36)	7	7	100	59.0	100	3970.0	2878.4	5475.7	2120.0	5895.0
				PIII(M48)	7	7	100	59.0	100	3032.3	1775.5	5178.6	1565.0	8003.0
			Total	PRE	56	7	12.5	5.2	24.1	4.6	4.2	5.2	<8.0	26.0
				PIII(M7)	56	56	100	93.6	100	22054.4	17406.0	27944.1	3932.0	149951.0
				PIII(M12)	56	56	100	93.6	100	7828.9	5954.0	10294.2	992.0	59262.0
				PIII(M18)	56	56	100	93.6	100	5307.0	4103.7	6863.1	600.0	37234.0
				PIII(M24)	55	55	100	93.5	100	4130.2	3163.3	5392.7	557.0	31073.0
				PIII(M36)	56	56	100	93.6	100	3503.0	2707.3	4532.5	428.0	30440.0
				PIII(M48)	56	56	100	93.6	100	2786.8	2149.9	3612.3	183.0	15706.0
		15_19y	S-	PRE	46	0	0.0	0.0	7.7	4.0	4.0	4.0	<8.0	<8.0
				PIII(M7)	46	46	100	92.3	100	13313.0	9759.7	18160.1	1322.0	148276.0
				PIII(M12)	45	45	100	92.1	100	4132.9	2958.2	5773.9	182.0	70532.0
				PIII(M18)	45	45	100	92.1	100	2608.5	1898.6	3584.0	116.0	31934.0
				PIII(M24)	45	45	100	92.1	100	2027.6	1479.0	2779.9	112.0	27936.0
				PIII(M36)	46	46	100	92.3	100	1786.7	1315.1	2427.5	73.0	23603.0
				PIII(M48)	46	46	100	92.3	100	1506.6	1111.9	2041.6	71.0	17426.0
			S+	PRE	3	3	100	29.2	100	41.1	1.6	1082.5	9.0	94.0
				PIII(M7)	3	3	100	29.2	100	21593.5	180.4	2585025	2482.0	99665.0
				PIII(M12)	3	3	100	29.2	100	10933.4	77.5	1543120	1156.0	51632.0
				PIII(M18)	3	3	100	29.2	100	9710.7	60.6	1555426	998.0	52061.0
				PIII(M24)	3	3	100	29.2	100	6949.9	53.8	897672.6	812.0	37420.0
				PIII(M36)	3	3	100	29.2	100	6620.7	47.3	927660.6	741.0	36109.0
				PIII(M48)	3	3	100	29.2	100	6001.7	64.1	561897.8	777.0	26218.0
			Total	PRE	49	3	6.1	1.3	16.9	4.6	3.9	5.5	<8.0	94.0
				PIII(M7)	49	49	100	92.7	100	13713.1	10020.3	18767.0	1322.0	148276.0
				PIII(M12)	48	48	100	92.6	100	4392.0	3120.6	6181.3	182.0	70532.0
				PIII(M18)	48	48	100	92.6	100	2831.9	2026.6	3957.2	116.0	52061.0
				PIII(M24)	48	48	100	92.6	100	2189.9	1575.4	3044.1	112.0	37420.0
				PIII(M36)	49	49	100	92.7	100	1935.9	1401.6	2673.9	73.0	36109.0
				PIII(M48)	49	49	100	92.7	100	1639.7	1192.0	2255.6	71.0	26218.0
		20_25y	S-	PRE	34	0	0.0	0.0	10.3	4.0	4.0	4.0	<8.0	<8.0
				PIII(M7)	34	34	100	89.7	100	10097.3	6946.1	14678.2	1810.0	125818.0
				PIII(M12)	34	34	100	89.7	100	3677.7	2524.7	5357.5	602.0	81240.0
				PIII(M18)	34	34	100	89.7	100	2462.9	1704.7	3558.4	494.0	45075.0
				PIII(M24)	34	34	100	89.7	100	1938.9	1337.8	2810.1	290.0	35172.0
				PIII(M36)	34	34	100	89.7	100	1607.5	1120.4	2306.3	350.0	20763.0
				PIII(M48)	34	34	100	89.7	100	1309.7	923.8	1856.9	251.0	17354.0
			S+	PRE	9	9	100	66.4	100	43.0	13.0	142.4	9.0	745.0

						≥ 8 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M7)	9	9	100	66.4	100	6852.8	3420.8	13728.3	2632.0	32551.0
				PIII(M12)	9	9	100	66.4	100	3158.0	1682.2	5928.5	1208.0	12328.0
				PIII(M18)	9	9	100	66.4	100	2408.4	1397.6	4150.3	951.0	7690.0
				PIII(M24)	9	9	100	66.4	100	1915.5	1040.0	3528.0	870.0	6645.0
				PIII(M36)	9	9	100	66.4	100	1672.6	938.5	2980.8	621.0	6198.0
				PIII(M48)	9	9	100	66.4	100	1491.0	798.5	2784.3	515.0	6343.0
			Total	PRE	43	9	20.9	10.0	36.0	6.6	4.6	9.5	<8.0	745.0
				PIII(M7)	43	43	100	91.8	100	9310.5	6757.7	12827.6	1810.0	125818.0
				PIII(M12)	43	43	100	91.8	100	3562.3	2600.7	4879.5	602.0	81240.0
				PIII(M18)	43	43	100	91.8	100	2451.4	1810.6	3319.0	494.0	45075.0
				PIII(M24)	43	43	100	91.8	100	1934.0	1419.7	2634.6	290.0	35172.0
				PIII(M36)	43	43	100	91.8	100	1620.9	1201.0	2187.5	350.0	20763.0
				PIII(M48)	43	43	100	91.8	100	1345.7	1002.6	1806.4	251.0	17354.0

V40_02 = HPV-16/18(40,40) AS04 0,2 m
V40_06 = HPV-16/18(40,40) AS04 0,6m
V20_06 = HPV-16/18(20,20) AS04 0,6 m
HPV = HPV-16/18(20,20) AS04 0,1,6m
S- = seronegative subjects (antibody concentration < 8 ELU/ML) prior to vaccination
S+ = seropositive subjects (antibody concentration ≥ 8 ELU/ML) prior to vaccination
GMT = geometric mean titers concentration calculated on all subjects
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with concentration equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = pre-vaccination
PII(M3) = Post Dose II, Month 3
PIII(M7) = Post Dose III, Month 7
PIII(M12) = Post Dose III, Month 12
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

Table 22 Number and percentage of subjects with an anti-HPV 18.VLP IGG concentration equal to or above the cut-off of 7 ELU/ML and GMTs by age stratum (Month 48 ATP Immunogenicity Cohort)

						≥ 7 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
HPV 18.VLP IGG	V40_02	9_14y	S-	PRE	56	0	0.0	0.0	6.4	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	56	56	100	93.6	100	4957.6	3982.5	6171.5	562.0	33045.0
				PIII(M7)	56	56	100	93.6	100	1108.8	857.4	1433.9	69.0	7965.0
				PIII(M12)	56	56	100	93.6	100	584.6	442.9	771.5	35.0	5521.0
				PIII(M18)	55	55	100	93.5	100	485.9	371.7	635.3	50.0	3262.0
				PIII(M24)	55	55	100	93.5	100	419.0	318.1	551.9	37.0	3257.0
				PIII(M36)	55	55	100	93.5	100	409.4	307.6	544.7	29.0	6446.0
				PIII(M48)	56	56	100	93.6	100	344.8	260.1	457.3	31.0	5240.0
			S+	PRE	5	5	100	47.8	100	15.7	8.9	27.9	8.0	24.0
				PII(M3)	5	5	100	47.8	100	4361.8	1615.3	11778.3	2098.0	14980.0
				PIII(M7)	5	5	100	47.8	100	962.8	365.5	2536.5	286.0	2502.0
				PIII(M12)	5	5	100	47.8	100	458.8	134.5	1564.7	111.0	1205.0
				PIII(M18)	5	5	100	47.8	100	382.4	122.1	1197.9	115.0	1292.0
				PIII(M24)	5	5	100	47.8	100	429.6	116.9	1579.1	89.0	1189.0
				PIII(M36)	5	5	100	47.8	100	418.5	83.5	2097.5	86.0	2081.0
				PIII(M48)	5	5	100	47.8	100	359.4	67.0	1927.0	81.0	2353.0
			Total	PRE	61	5	8.2	2.7	18.1	4.0	3.5	4.4	<7.0	24.0
				PII(M3)	61	61	100	94.1	100	4905.9	3986.2	6037.7	562.0	33045.0
				PIII(M7)	61	61	100	94.1	100	1096.0	861.1	1395.0	69.0	7965.0
				PIII(M12)	61	61	100	94.1	100	573.1	440.6	745.3	35.0	5521.0
				PIII(M18)	60	60	100	94.0	100	476.3	369.7	613.6	50.0	3262.0
				PIII(M24)	60	60	100	94.0	100	419.8	323.2	545.4	37.0	3257.0
				PIII(M36)	60	60	100	94.0	100	410.1	311.4	540.1	29.0	6446.0
				PIII(M48)	61	61	100	94.1	100	346.0	263.2	454.8	31.0	5240.0
		15_19y	S-	PRE	50	0	0.0	0.0	7.1	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	50	50	100	92.9	100	2946.2	2233.7	3886.1	148.0	22529.0
				PIII(M7)	50	50	100	92.9	100	633.1	490.6	816.9	107.0	4507.0
				PIII(M12)	50	50	100	92.9	100	364.5	277.5	478.8	40.0	2969.0
				PIII(M18)	50	50	100	92.9	100	278.1	212.0	364.9	42.0	2259.0
				PIII(M24)	48	48	100	92.6	100	228.9	172.9	303.0	26.0	1823.0
				PIII(M36)	49	49	100	92.7	100	227.6	166.5	311.2	18.0	1633.0
				PIII(M48)	50	50	100	92.9	100	195.3	143.7	265.4	12.0	1276.0
			S+	PRE	4	4	100	39.8	100	25.7	4.4	149.2	8.0	114.0
				PII(M3)	4	4	100	39.8	100	10395.4	2701.9	39995.7	4727.0	33321.0
				PIII(M7)	4	4	100	39.8	100	2838.7	1011.5	7966.5	1864.0	7467.0
				PIII(M12)	4	4	100	39.8	100	1257.2	426.7	3704.4	779.0	3415.0
				PIII(M18)	4	4	100	39.8	100	1220.6	317.7	4689.7	543.0	3091.0
				PIII(M24)	4	4	100	39.8	100	930.6	274.4	3156.2	493.0	2332.0
				PIII(M36)	4	4	100	39.8	100	707.8	228.4	2193.9	403.0	1826.0
				PIII(M48)	4	4	100	39.8	100	650.8	196.2	2159.4	325.0	1700.0
			Total	PRE	54	4	7.4	2.1	17.9	4.1	3.5	4.8	<7.0	114.0
				PII(M3)	54	54	100	93.4	100	3234.7	2452.3	4266.7	148.0	33321.0
				PIII(M7)	54	54	100	93.4	100	707.5	544.2	919.9	107.0	7467.0
				PIII(M12)	54	54	100	93.4	100	399.5	304.7	523.8	40.0	3415.0
				PIII(M18)	54	54	100	93.4	100	310.3	235.0	409.7	42.0	3091.0
				PIII(M24)	52	52	100	93.2	100	255.0	192.0	338.5	26.0	2332.0

						≥ 7 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M36)	53	53	100	93.3	100	248.0	183.0	336.0	18.0	1826.0
				PIII(M48)	54	54	100	93.4	100	213.5	158.1	288.3	12.0	1700.0
		20_25y	S-	PRE	32	0	0.0	0.0	10.9	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	32	32	100	89.1	100	2994.6	2133.2	4203.7	443.0	19057.0
				PIII(M7)	32	32	100	89.1	100	632.1	438.9	910.2	73.0	3027.0
				PIII(M12)	32	32	100	89.1	100	345.4	232.3	513.7	25.0	1678.0
				PIII(M18)	31	31	100	88.8	100	308.0	203.9	465.4	15.0	1591.0
				PIII(M24)	30	30	100	88.4	100	273.1	180.6	412.9	12.0	1568.0
				PIII(M36)	31	31	100	88.8	100	244.7	163.1	367.2	10.0	2104.0
				PIII(M48)	32	32	100	89.1	100	232.2	151.6	355.6	9.0	1924.0
			S+	PRE	13	13	100	75.3	100	21.9	9.6	50.3	7.0	510.0
				PII(M3)	13	13	100	75.3	100	2207.5	1540.9	3162.7	671.0	4154.0
				PIII(M7)	13	13	100	75.3	100	660.7	386.5	1129.3	155.0	2427.0
				PIII(M12)	13	13	100	75.3	100	410.5	216.5	778.3	84.0	1594.0
				PIII(M18)	13	13	100	75.3	100	348.5	182.1	667.1	63.0	1298.0
				PIII(M24)	13	13	100	75.3	100	317.6	163.2	618.1	46.0	1112.0
				PIII(M36)	13	13	100	75.3	100	231.5	117.9	454.4	35.0	1075.0
				PIII(M48)	13	13	100	75.3	100	207.4	103.0	417.2	28.0	798.0
			Total	PRE	45	13	28.9	16.4	44.3	5.9	4.3	8.3	<7.0	510.0
				PII(M3)	45	45	100	92.1	100	2742.1	2117.7	3550.5	443.0	19057.0
				PIII(M7)	45	45	100	92.1	100	640.2	478.8	856.2	73.0	3027.0
				PIII(M12)	45	45	100	92.1	100	363.1	262.5	502.2	25.0	1678.0
				PIII(M18)	44	44	100	92.0	100	319.5	228.7	446.3	15.0	1591.0
				PIII(M24)	43	43	100	91.8	100	285.8	204.1	400.3	12.0	1568.0
				PIII(M36)	44	44	100	92.0	100	240.7	172.5	336.0	10.0	2104.0
				PIII(M48)	45	45	100	92.1	100	224.7	158.4	318.7	9.0	1924.0
	V40_06	9_14y	S-	PRE	51	0	0.0	0.0	7.0	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	51	51	100	93.0	100	270.4	206.8	353.6	46.0	3159.0
				PIII(M7)	51	51	100	93.0	100	8863.3	7099.7	11065.2	1202.0	60059.0
				PIII(M12)	51	51	100	93.0	100	2193.3	1690.9	2845.0	361.0	20569.0
				PIII(M18)	51	51	100	93.0	100	1254.7	959.7	1640.4	193.0	11555.0
				PIII(M24)	50	50	100	92.9	100	957.7	727.0	1261.6	184.0	6809.0
				PIII(M36)	51	51	100	93.0	100	765.3	585.0	1001.1	124.0	4814.0
				PIII(M48)	51	51	100	93.0	100	683.5	518.3	901.4	119.0	7909.0
			Total	PRE	51	0	0.0	0.0	7.0	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	51	51	100	93.0	100	270.4	206.8	353.6	46.0	3159.0
				PIII(M7)	51	51	100	93.0	100	8863.3	7099.7	11065.2	1202.0	60059.0
				PIII(M12)	51	51	100	93.0	100	2193.3	1690.9	2845.0	361.0	20569.0
				PIII(M18)	51	51	100	93.0	100	1254.7	959.7	1640.4	193.0	11555.0
				PIII(M24)	50	50	100	92.9	100	957.7	727.0	1261.6	184.0	6809.0
				PIII(M36)	51	51	100	93.0	100	765.3	585.0	1001.1	124.0	4814.0
				PIII(M48)	51	51	100	93.0	100	683.5	518.3	901.4	119.0	7909.0
		15_19y	S-	PRE	48	0	0.0	0.0	7.4	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	48	48	100	92.6	100	222.3	164.7	299.9	38.0	7952.0
				PIII(M7)	48	48	100	92.6	100	6964.5	5413.5	8959.8	412.0	91976.0
				PIII(M12)	48	48	100	92.6	100	2253.8	1686.0	3012.8	190.0	34743.0
				PIII(M18)	48	48	100	92.6	100	1301.4	955.7	1772.2	102.0	19845.0
				PIII(M24)	47	47	100	92.5	100	1032.7	763.0	1397.7	73.0	15066.0
				PIII(M36)	48	48	100	92.6	100	856.9	625.2	1174.4	50.0	15050.0
				PIII(M48)	48	48	100	92.6	100	726.1	537.4	981.2	45.0	10456.0
			S+	PRE	3	3	100	29.2	100	31.4	0.1	7024.8	8.0	387.0

						≥ 7 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PII(M3)	3	3	100	29.2	100	5670.5	129.9	247600.7	1144.0	23563.0
				PIII(M7)	3	3	100	29.2	100	11224.3	3855.0	32681.1	6856.0	15146.0
				PIII(M12)	3	3	100	29.2	100	5698.8	1155.5	28106.3	2797.0	9748.0
				PIII(M18)	2	2	100	15.8	100	4461.0	3.7	5386891	2552.0	7798.0
				PIII(M24)	3	3	100	29.2	100	2514.5	165.7	38151.5	1007.0	8456.0
				PIII(M36)	3	3	100	29.2	100	2118.9	155.2	28936.2	942.0	6960.0
				PIII(M48)	3	3	100	29.2	100	1937.4	159.8	23489.1	1032.0	6170.0
			Total	PRE	51	3	5.9	1.2	16.2	4.0	3.3	4.8	<7.0	387.0
				PII(M3)	51	51	100	93.0	100	269.0	186.7	387.5	38.0	23563.0
				PIII(M7)	51	51	100	93.0	100	7162.8	5634.7	9105.2	412.0	91976.0
				PIII(M12)	51	51	100	93.0	100	2380.2	1795.6	3155.2	190.0	34743.0
				PIII(M18)	50	50	100	92.9	100	1367.2	1007.1	1856.0	102.0	19845.0
				PIII(M24)	50	50	100	92.9	100	1089.3	809.4	1466.0	73.0	15066.0
				PIII(M36)	51	51	100	93.0	100	903.7	664.2	1229.6	50.0	15050.0
				PIII(M48)	51	51	100	93.0	100	769.3	572.4	1033.9	45.0	10456.0
		20_25y	S-	PRE	40	0	0.0	0.0	8.8	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	40	40	100	91.2	100	174.9	122.7	249.2	13.0	2442.0
				PIII(M7)	40	40	100	91.2	100	4663.9	3544.0	6137.8	845.0	34350.0
				PIII(M12)	39	39	100	91.0	100	1225.8	912.7	1646.4	233.0	10669.0
				PIII(M18)	38	38	100	90.7	100	712.6	515.3	985.3	103.0	6285.0
				PIII(M24)	39	39	100	91.0	100	570.8	421.3	773.5	90.0	4062.0
				PIII(M36)	38	38	100	90.7	100	532.2	392.9	720.8	57.0	3260.0
				PIII(M48)	40	40	100	91.2	100	421.9	312.4	569.8	46.0	3204.0
			S+	PRE	11	11	100	71.5	100	23.3	11.2	48.2	9.0	210.0
				PII(M3)	11	11	100	71.5	100	675.7	308.0	1482.2	152.0	9081.0
				PIII(M7)	11	11	100	71.5	100	5896.1	2689.0	12928.4	619.0	25115.0
				PIII(M12)	11	11	100	71.5	100	2070.0	948.7	4516.9	240.0	9524.0
				PIII(M18)	11	11	100	71.5	100	1288.8	586.8	2830.6	218.0	5313.0
				PIII(M24)	10	10	100	69.2	100	1128.0	490.6	2593.7	155.0	4545.0
				PIII(M36)	11	11	100	71.5	100	824.6	345.4	1968.6	116.0	4368.0
				PIII(M48)	11	11	100	71.5	100	677.2	294.0	1559.5	95.0	3954.0
			Total	PRE	51	11	21.6	11.3	35.3	5.3	4.1	6.8	<7.0	210.0
				PII(M3)	51	51	100	93.0	100	234.1	165.0	332.0	13.0	9081.0
				PIII(M7)	51	51	100	93.0	100	4905.8	3780.8	6365.6	619.0	34350.0
				PIII(M12)	50	50	100	92.9	100	1375.6	1040.4	1818.7	233.0	10669.0
				PIII(M18)	49	49	100	92.7	100	814.0	602.5	1099.8	103.0	6285.0
				PIII(M24)	49	49	100	92.7	100	656.0	490.4	877.5	90.0	4545.0
				PIII(M36)	49	49	100	92.7	100	587.1	438.0	787.0	57.0	4368.0
				PIII(M48)	51	51	100	93.0	100	467.2	351.0	622.1	46.0	3954.0
	V20_06	9_14y	S-	PRE	52	0	0.0	0.0	6.8	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	52	52	100	93.2	100	211.8	156.9	285.8	41.0	5333.0
				PIII(M7)	52	52	100	93.2	100	5778.5	4786.5	6976.1	1094.0	36047.0
				PIII(M12)	52	52	100	93.2	100	1624.3	1284.7	2053.6	178.0	11420.0
				PIII(M18)	52	52	100	93.2	100	936.6	736.8	1190.7	95.0	5228.0
				PIII(M24)	51	51	100	93.0	100	727.7	570.8	927.6	92.0	4440.0
				PIII(M36)	50	50	100	92.9	100	646.0	500.3	834.0	103.0	5844.0
				PIII(M48)	52	52	100	93.2	100	542.9	426.5	691.0	103.0	2928.0
			S+	PRE	3	3	100	29.2	100	8.0	5.8	10.9	7.0	9.0
				PII(M3)	3	3	100	29.2	100	207.3	76.6	561.3	140.0	312.0
				PIII(M7)	3	3	100	29.2	100	8010.4	2256.9	28431.7	4474.0	11551.0
				PIII(M12)	3	3	100	29.2	100	2115.0	502.1	8908.4	1102.0	3329.0

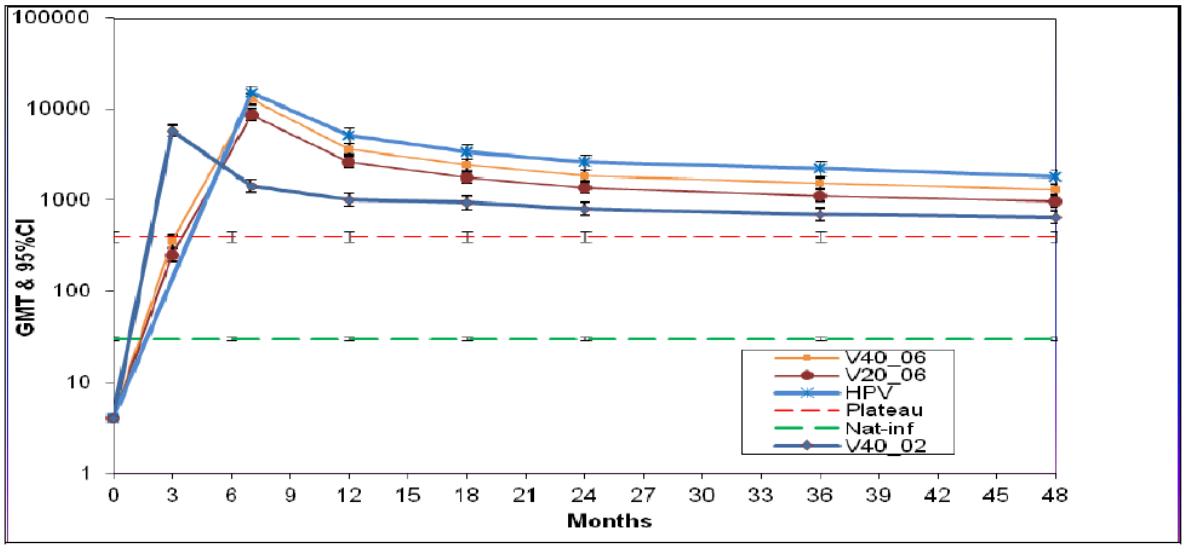
						≥ 7 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M18)	3	3	100	29.2	100	1075.2	277.2	4169.8	636.0	1890.0
				PIII(M24)	3	3	100	29.2	100	909.5	327.0	2529.1	678.0	1456.0
				PIII(M36)	3	3	100	29.2	100	686.4	188.7	2497.3	457.0	1233.0
				PIII(M48)	3	3	100	29.2	100	597.2	314.0	1135.5	482.0	796.0
			Total	PRE	55	3	5.5	1.1	15.1	3.7	3.5	3.9	<7.0	9.0
				PII(M3)	55	55	100	93.5	100	211.5	159.3	280.9	41.0	5333.0
				PIII(M7)	55	55	100	93.5	100	5882.4	4909.2	7048.4	1094.0	36047.0
				PIII(M12)	55	55	100	93.5	100	1647.8	1317.2	2061.5	178.0	11420.0
				PIII(M18)	55	55	100	93.5	100	943.7	751.0	1185.9	95.0	5228.0
				PIII(M24)	54	54	100	93.4	100	736.7	585.2	927.5	92.0	4440.0
				PIII(M36)	53	53	100	93.3	100	648.2	508.8	825.9	103.0	5844.0
				PIII(M48)	55	55	100	93.5	100	545.7	434.4	685.6	103.0	2928.0
		15_19y	S-	PRE	48	0	0.0	0.0	7.4	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	48	48	100	92.6	100	208.3	148.5	292.2	26.0	4646.0
				PIII(M7)	48	48	100	92.6	100	5553.1	4524.7	6815.2	1746.0	34562.0
				PIII(M12)	48	48	100	92.6	100	1640.8	1291.8	2084.2	231.0	10163.0
				PIII(M18)	48	48	100	92.6	100	1059.5	829.2	1353.9	117.0	5847.0
				PIII(M24)	47	47	100	92.5	100	839.7	659.2	1069.5	120.0	4669.0
				PIII(M36)	48	48	100	92.6	100	746.7	580.6	960.4	86.0	3297.0
				PIII(M48)	48	48	100	92.6	100	633.6	487.8	823.0	91.0	3668.0
			S+	PRE	4	4	100	39.8	100	20.7	5.1	84.7	11.0	72.0
				PII(M3)	4	4	100	39.8	100	720.6	58.1	8929.2	124.0	4199.0
				PIII(M7)	4	4	100	39.8	100	3307.1	1186.0	9221.6	1851.0	8252.0
				PIII(M12)	4	4	100	39.8	100	712.1	412.1	1230.6	518.0	1000.0
				PIII(M18)	3	3	100	29.2	100	454.7	175.5	1177.5	324.0	689.0
				PIII(M24)	4	4	100	39.8	100	413.8	246.1	695.6	272.0	586.0
				PIII(M36)	4	4	100	39.8	100	384.8	175.7	842.5	227.0	747.0
				PIII(M48)	4	4	100	39.8	100	290.3	167.6	502.8	242.0	487.0
			Total	PRE	52	4	7.7	2.1	18.5	4.0	3.5	4.6	<7.0	72.0
				PII(M3)	52	52	100	93.2	100	229.1	162.7	322.6	26.0	4646.0
				PIII(M7)	52	52	100	93.2	100	5336.1	4380.5	6500.0	1746.0	34562.0
				PIII(M12)	52	52	100	93.2	100	1538.8	1222.6	1936.8	231.0	10163.0
				PIII(M18)	51	51	100	93.0	100	1008.1	794.5	1279.0	117.0	5847.0
				PIII(M24)	51	51	100	93.0	100	794.3	631.2	999.6	120.0	4669.0
				PIII(M36)	52	52	100	93.2	100	709.6	558.6	901.4	86.0	3297.0
				PIII(M48)	52	52	100	93.2	100	596.7	465.2	765.3	91.0	3668.0
		20_25y	S-	PRE	35	0	0.0	0.0	10.0	3.5	3.5	3.5	<7.0	<7.0
				PII(M3)	35	35	100	90.0	100	125.3	85.9	182.7	16.0	757.0
				PIII(M7)	35	35	100	90.0	100	4357.2	3091.2	6141.6	551.0	24791.0
				PIII(M12)	35	35	100	90.0	100	1159.5	768.3	1749.9	99.0	6105.0
				PIII(M18)	35	35	100	90.0	100	711.3	469.8	1076.9	45.0	4618.0
				PIII(M24)	34	34	100	89.7	100	565.4	373.6	855.8	43.0	3424.0
				PIII(M36)	34	34	100	89.7	100	474.6	308.7	729.7	30.0	2911.0
				PIII(M48)	35	35	100	90.0	100	399.0	267.1	596.1	33.0	2075.0
			S+	PRE	15	15	100	78.2	100	24.9	13.5	46.2	7.0	141.0
				PII(M3)	15	15	100	78.2	100	410.2	208.6	806.7	98.0	3482.0
				PIII(M7)	15	15	100	78.2	100	4782.5	3171.9	7210.9	2018.0	18651.0
				PIII(M12)	15	15	100	78.2	100	1646.0	1093.4	2477.9	499.0	7031.0
				PIII(M18)	15	15	100	78.2	100	957.0	628.5	1457.3	258.0	3527.0
				PIII(M24)	15	15	100	78.2	100	743.6	503.1	1099.1	209.0	2956.0
				PIII(M36)	14	14	100	76.8	100	604.4	388.3	940.6	152.0	2292.0

						≥7 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
				PIII(M48)	15	15	100	78.2	100	471.9	318.9	698.5	155.0	1568.0
			Total	PRE	50	15	30.0	17.9	44.6	6.3	4.6	8.6	<7.0	141.0
				PII(M3)	50	50	100	92.9	100	178.8	125.3	255.1	16.0	3482.0
				PIII(M7)	50	50	100	92.9	100	4480.7	3446.9	5824.5	551.0	24791.0
				PIII(M12)	50	50	100	92.9	100	1288.0	946.1	1753.4	99.0	7031.0
				PIII(M18)	50	50	100	92.9	100	777.5	569.8	1060.8	45.0	4618.0
				PIII(M24)	49	49	100	92.7	100	614.9	453.0	834.6	43.0	3424.0
				PIII(M36)	48	48	100	92.6	100	509.3	368.5	703.9	30.0	2911.0
				PIII(M48)	50	50	100	92.9	100	419.6	311.6	565.1	33.0	2075.0
	HPV	9_14y	S-	PRE	50	0	0.0	0.0	7.1	3.5	3.5	3.5	<7.0	<7.0
				PIII(M7)	50	50	100	92.9	100	7685.5	6024.5	9804.6	1680.0	37491.0
				PIII(M12)	50	50	100	92.9	100	2562.4	1877.7	3497.0	339.0	19004.0
				PIII(M18)	50	50	100	92.9	100	1617.6	1213.5	2156.3	247.0	8773.0
				PIII(M24)	49	49	100	92.7	100	1323.9	985.1	1779.1	187.0	8369.0
				PIII(M36)	50	50	100	92.9	100	1166.6	879.0	1548.4	139.0	8194.0
				PIII(M48)	50	50	100	92.9	100	954.7	716.9	1271.4	101.0	6125.0
			S+	PRE	6	6	100	54.1	100	15.9	7.6	33.6	8.0	43.0
				PIII(M7)	6	6	100	54.1	100	6112.6	3530.0	10584.4	2806.0	11503.0
				PIII(M12)	6	6	100	54.1	100	2149.9	1183.2	3906.5	687.0	3126.0
				PIII(M18)	6	6	100	54.1	100	1519.1	787.4	2930.4	466.0	2997.0
				PIII(M24)	6	6	100	54.1	100	1206.3	635.7	2289.1	420.0	2477.0
				PIII(M36)	6	6	100	54.1	100	1207.2	641.8	2270.5	475.0	2582.0
				PIII(M48)	6	6	100	54.1	100	864.1	440.1	1696.5	302.0	1976.0
			Total	PRE	56	6	10.7	4.0	21.9	4.1	3.6	4.7	<7.0	43.0
				PIII(M7)	56	56	100	93.6	100	7499.2	6009.3	9358.6	1680.0	37491.0
				PIII(M12)	56	56	100	93.6	100	2514.7	1899.2	3329.7	339.0	19004.0
				PIII(M18)	56	56	100	93.6	100	1606.7	1238.1	2085.2	247.0	8773.0
				PIII(M24)	55	55	100	93.5	100	1310.5	1003.3	1711.8	187.0	8369.0
				PIII(M36)	56	56	100	93.6	100	1170.9	906.0	1513.2	139.0	8194.0
				PIII(M48)	56	56	100	93.6	100	944.6	728.2	1225.2	101.0	6125.0
		15_19y	S-	PRE	45	0	0.0	0.0	7.9	3.5	3.5	3.5	<7.0	<7.0
				PIII(M7)	45	45	100	92.1	100	4986.1	3756.5	6618.0	1144.0	69885.0
				PIII(M12)	44	44	100	92.0	100	1502.9	1080.2	2091.0	167.0	25737.0
				PIII(M18)	44	44	100	92.0	100	1019.3	720.9	1441.3	65.0	19963.0
				PIII(M24)	44	44	100	92.0	100	826.3	585.9	1165.5	39.0	10419.0
				PIII(M36)	45	45	100	92.1	100	746.2	524.1	1062.6	25.0	9702.0
				PIII(M48)	45	45	100	92.1	100	594.4	416.5	848.2	18.0	7278.0
			S+	PRE	4	4	100	39.8	100	11.5	6.9	19.4	8.0	17.0
				PIII(M7)	4	4	100	39.8	100	5026.7	227.9	110872.8	926.0	81284.0
				PIII(M12)	4	4	100	39.8	100	2001.4	59.2	67646.6	363.0	47033.0
				PIII(M18)	4	4	100	39.8	100	1129.1	30.6	41675.9	197.0	29745.0
				PIII(M24)	4	4	100	39.8	100	984.0	29.7	32610.1	176.0	24394.0
				PIII(M36)	4	4	100	39.8	100	973.8	29.4	32256.0	206.0	24703.0
				PIII(M48)	4	4	100	39.8	100	797.9	22.9	27860.2	168.0	21133.0
			Total	PRE	49	4	8.2	2.3	19.6	3.9	3.5	4.3	<7.0	17.0
				PIII(M7)	49	49	100	92.7	100	4989.4	3717.0	6697.3	926.0	81284.0
				PIII(M12)	48	48	100	92.6	100	1539.2	1091.8	2169.7	167.0	47033.0
				PIII(M18)	48	48	100	92.6	100	1028.1	719.0	1470.1	65.0	29745.0
				PIII(M24)	48	48	100	92.6	100	838.5	588.8	1194.0	39.0	24394.0
				PIII(M36)	49	49	100	92.7	100	762.6	531.7	1093.8	25.0	24703.0
				PIII(M48)	49	49	100	92.7	100	608.8	423.2	875.9	18.0	21133.0

						≥ 7 ELU/ML				GMT				
								95% CI			95% CI			
Antibody	Group	Sub-group	Pre-vacc status	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
		20_25y	S-	PRE	34	0	0.0	0.0	10.3	3.5	3.5	3.5	<7.0	<7.0
				PIII(M7)	34	34	100	89.7	100	4213.9	3089.1	5748.2	1030.0	48127.0
				PIII(M12)	34	34	100	89.7	100	1609.1	1140.2	2270.9	289.0	26768.0
				PIII(M18)	34	34	100	89.7	100	1027.7	729.2	1448.5	151.0	15458.0
				PIII(M24)	34	34	100	89.7	100	806.9	566.6	1149.3	96.0	13295.0
				PIII(M36)	34	34	100	89.7	100	720.7	504.8	1029.0	70.0	9202.0
				PIII(M48)	34	34	100	89.7	100	618.2	450.0	849.3	141.0	7320.0
			S+	PRE	9	9	100	66.4	100	16.2	7.7	34.1	7.0	130.0
				PIII(M7)	9	9	100	66.4	100	3807.1	1892.2	7659.8	1891.0	34621.0
				PIII(M12)	9	9	100	66.4	100	1397.6	695.3	2809.6	564.0	10702.0
				PIII(M18)	9	9	100	66.4	100	1120.1	614.6	2041.3	507.0	6262.0
				PIII(M24)	9	9	100	66.4	100	786.2	382.2	1617.3	289.0	4519.0
				PIII(M36)	9	9	100	66.4	100	714.8	349.8	1460.5	289.0	3701.0
				PIII(M48)	9	9	100	66.4	100	633.9	298.7	1345.5	179.0	3194.0
			Total	PRE	43	9	20.9	10.0	36.0	4.8	3.8	6.1	<7.0	130.0
				PIII(M7)	43	43	100	91.8	100	4125.3	3142.7	5415.2	1030.0	48127.0
				PIII(M12)	43	43	100	91.8	100	1562.4	1161.8	2101.0	289.0	26768.0
				PIII(M18)	43	43	100	91.8	100	1046.4	784.3	1396.0	151.0	15458.0
				PIII(M24)	43	43	100	91.8	100	802.6	592.2	1087.5	96.0	13295.0
				PIII(M36)	43	43	100	91.8	100	719.5	530.2	976.2	70.0	9202.0
				PIII(M48)	43	43	100	91.8	100	621.5	469.2	823.1	141.0	7320.0

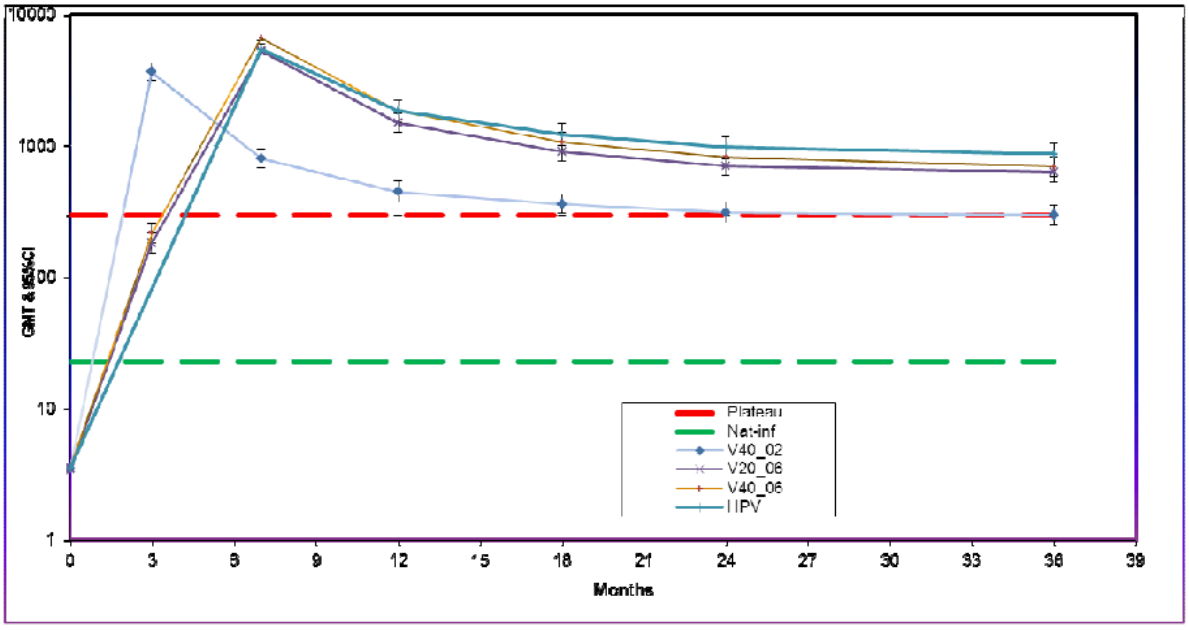
V40_02 = HPV-16/18(40,40) AS04 0,2 m
V40_06 = HPV-16/18(40,40) AS04 0,6m
V20_06 = HPV-16/18(20,20) AS04 0,6 m
HPV = HPV-16/18(20,20) AS04 0,1,6m
S- = seronegative subjects (antibody concentration < 7 ELU/ML) prior to vaccination
S+ = seropositive subjects (antibody concentration ≥ 7 ELU/ML) prior to vaccination
GMT = geometric mean titers concentration calculated on all subjects
N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with concentration equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = pre-vaccination
PII(M3) = Post Dose II, Month 3
PIII(M7) = Post Dose III, Month 7
PIII(M12) = Post Dose III, Month 12
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

Figure 1 Persistence of HPV-16 antibody titers (ELISA) in subjects seronegative at baseline (Month 48 ATP Immunogenicity Cohort)



V40_02 = HPV-16/18(40,40) AS04 0,2 m;
V40_06 = HPV-16/18(40,40) AS04 0,6 m;
V20_06 = HPV-16/18(20,20) AS04 0,6 m;
HPV = HPV-16/18(20,20) AS04 0,1,6 m;
Nat-inf =Subjects who had cleared HPV-16 infection had GMTs of 29.8 EL.U/mL (95% CI: [28.5; 31.1]) in Study HPV-008;
Plateau = The GMTs at the plateau level in Study HPV-007 (Month 45-50 time point) were 397.8 EL.U/mL (95% CI: [344.7; 459.1]) for HPV-16 antibodies.

Figure 2 Persistence of HPV-18 antibody titers (ELISA) in subjects seronegative at baseline (Month 48 ATP Immunogenicity Cohort)



V40_02 = HPV-16/18(40,40) AS04 0,2 m;
V40_06 = HPV-16/18(40,40) AS04 0,6 m;
V20_06 = HPV-16/18(20,20) AS04 0,6 m;
HPV = HPV-16/18(20,20) AS04 0,1,6 m;
Nat-inf = Subjects who had cleared HPV-18 infection had GMTs of 22.7 EL.U/mL (95% CI: [21.7; 23.7]) in Study HPV-008;
Plateau = The GMTs at the plateau level in Study HPV-007 (Month 45-50 time point) were 297.3 EL.U/mL (95% CI: [258.2; 342.2]) for HPV-18 antibodies.

Safety results

During the follow-up period from Month 36 to Month 48, 18 SAEs were reported in 15 subjects.

46 subjects reported at least one medically significant condition (MSC), 11 subjects reported at least one new onset chronic disease (NOCD), 2 subjects reported at least one new onset autoimmune disease (NOAD).

4. MAH'S OVERALL CONCLUSION

The data submitted confirm a sustained immune response up to 48 months after the first vaccine dose administration and the findings remain in line with those observed at previous time points. The benefit-risk balance for Cervarix remains positive. No further regulatory action is required.

5. RAPPORTEUR's CONCLUSION

The MAH's conclusion is endorsed.

6. REQUEST FOR SUPPLEMENTARY INFORMATION

The MAH is requested to submit the Month 60 follow-up study report of study HPV-048 in due time (expected October 2013).