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.: 104389 (MeMuRu-OKA/044)

Title: A phase III, blinded, randomized, controlled study to evaluate the immunogenicity and safety of three production lots of GlaxoSmithKline Biologicals' combined measles-mumps-rubella-varicella (MeMuRu-OKA) candidate vaccine given on a two-dose schedule to healthy children in their second year of life.
MeMuRu-OKA: GlaxoSmithKline (GSK) Biologicals' combined measles, mumps, rubella and varicella vaccine.

Rationale: The aim of this study was to evaluate the consistency of 3 production lots of the MeMuRu-OKA vaccine and to rule out a mumps seroconversion rate of less than 90% for the pooled lots of MeMuRu-OKA vaccine after the first dose. GSK Biologicals' *Priorix* and *Varilrix* were used as benchmarks.

MMR *(Priorix)*: GSK Biologicals' measles-mumps-rubella vaccine,
V (*Varilrix)*: GSK Biologicals' varicella vaccine.

Phase: III

Study Period: 10 May 2005 to 08 December 2005.

Study Design: Randomized (1:1:1:1), partially blinded*, controlled, self-contained study with 4 parallel groups.
*The study was carried out in a double-blind manner with respect to the 3 MeMuRu-OKA lots, open with respect to Groups MeMuRu-OKA lots A-B-C versus Group MMR_V.

Centers: 81 study centers in Germany

Indication: Active immunization of healthy children during their second year of life against measles, mumps, rubella and varicella diseases.

Treatment: The study groups were as follows:

- Group MMRV_1 received two doses of MeMuRu-OKA vaccine lot A, one at Day 0 and one at Week 6,
- Group MMRV_2 received two doses of MeMuRu-OKA vaccine lot B, one at Day 0 and one at Week 6,
- Group MMRV_3 received two doses of MeMuRu-OKA vaccine lot C, one at Day 0 and one at Week 6,
- Group MMR+V received one dose of a MMR vaccine administered concomitantly with one dose of V vaccine at Day 0 and a second dose of MMR vaccine in Week 6.

Vaccines were administered subcutaneously in the deltoid region (MeMuRu-OKA and MMR vaccines in the left arm and varicella vaccine in the right arm).
For the data analyses, MMRV_1, MMRV_2 and MMRV_3 were pooled into MMRV Group.

Objectives:

- To demonstrate the consistency of 3 production lots of the MeMuRu-OKA candidate vaccine in terms of measles, mumps*, rubella and varicella seroconversion after the first dose.
- To rule out a mumps* seroconversion rate below 90% for the pooled lots of MeMuRu-OKA vaccine after the first dose.

* Mumps seroconversion rate by neutralization assay.

Primary Outcome/Efficacy Variable:
Seroconversion rates for measles, mumps*, rubella and varicella approximately 42-56 days after the first dose.
Cut-off values for seroconversion:

- Measles: 150 mIU/mL

- Mumps: 28 End point dilution$_{50}$ (ED_{50}) by neutralization assay
- Rubella: 4 IU/mL
- Varicella: 1:4 titration dilution

* Mumps seroconversion rate by neutralization assay

Secondary Outcome/Efficacy Variable(s):

Immunogenicity

- Mumps seroconversion rate by Enzyme-Linked Immunoassay (ELISA), 42-56 days after the first dose. Cut-off values for seroconversion: 231 U/mL by ELISA
- Measles, mumps**, rubella and varicella seroconversion rates, 42-56 days after the second dose.
- Measles, mumps, rubella and varicella antibody titers, 42-56 days after the first and second dose.

** Mumps seroconversion rate by neutralization assay and ELISA.

Safety

- Occurrence of any and Grade 3 solicited local symptoms (injection site redness, pain and swelling) within 4 days (Day 0-3) after each vaccination.
- Occurrence of any, Grade 3 and vaccine-related solicited general symptoms within 43 days (Day 0-42) after each vaccination in terms of fever, rash, any sign of meningitis including febrile convulsion and parotitis.
- Occurrence of any, severe and vaccine-related unsolicited symptoms within 43 days (Day 0-42) after each vaccination.
- Occurrence of serious adverse events (SAEs) throughout the entire study period (Day 0 to Week 12).

Statistical Methods:

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

- The Total Vaccinated Cohort included all vaccinated subjects for whom data were available.
- The ATP Cohort for immunogenicity included all subjects who received at least one dose of study/comparator vaccine, who had not received a vaccine not specified or forbidden in the protocol, for whom the administration route of study vaccine(s) was correct, with pre-vaccination and with post Dose 1 serology data available for at least one of the vaccine antigens and who complied with protocol procedures.

Analysis of immunogenicity:

The analysis was performed on the ATP Cohort for immunogenicity.

Inferential analysis

To demonstrate the consistency of 3 lots of the study vaccine, the pair wise standardized asymptotic 95% Confidence Intervals (CIs) for seroconversion rate difference between the lots were computed for each antigen (measles, mumps, rubella and varicella) after the first dose. The 3 lots were considered consistent if, for each antigen and each pair wise comparison, the standardized asymptotic 95% CI was included between [-10%, 10%].

To rule out a mumps seroconversion rate below 90% (as measured by neutralization assay) for the pooled lots of the study vaccine after the first dose, data from the three lots were pooled and the null hypothesis was rejected if the lower limit of the exact 95% CI for mumps seroconversion rate post Dose 1 for the pooled lots was at least 90% in initially seronegative subjects.

Descriptive analysis

For each group and for the 3 study vaccine lots pooled, at each blood sampling time point, seroconversion rates with exact 95% CIs and geometric mean titers (GMTs) with 95% CIs were calculated for each antigen after each dose for initially seronegative (subjects with titers < specified cut-off) subjects . Subjects without a pre-vaccination result were not included in the analysis.

Analysis of safety

The analysis was performed on the Total Vaccinated Cohort.

The number and percentage of subjects (with exact 95% CIs) with each local solicited symptom (any

and Grade 3) during the 4-day (Day 0-3) follow-up period after each vaccination were tabulated for each group and for the pooled study vaccine lots. The number and percentage of subjects with each general solicited symptom (any, Grade 3 and related) during the 43-day (Day 0-42) follow-up period after each vaccination were tabulated for each group and for the pooled study vaccine lots. The number and percentage of subjects with unsolicited adverse events (AEs) (any, severe and related) during the 43-day (Day 0-42) follow-up period after each vaccination were tabulated per group and for the pooled study vaccine lots according to the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms. The occurrence of SAEs during the entire study period was tabulated per group according to the MedDRA preferred terms.

Study Population: Subjects were male or female infants between 11 and 21 months of age at the time of the first vaccination, free of obvious health problems as established by medical history and clinical examination before entering into the study. Subjects with a history of measles, mumps, and rubella and/or varicella/zoster diseases or with known exposure to measles, mumps, rubella and/or varicella/zoster within 30 days prior to the start of the study were excluded. Written informed consent was obtained from the parents or guardians of the subject prior to study entry.

Number of Subjects:	**MMRV_1**	**MMRV_2**	**MMRV_3**	**MMRV**	**MMR+V**
Planned, N	236	236	236	708	236
Randomized, N (Total Vaccinated Cohort)	246	248	238	732	238
Completed, n (%)	237 (96.3)	245 (98.8)	232 (97.5)	714 (97.5)	233 (97.9)
Total Number Subjects Withdrawn, n (%)	9 (3.7)	3 (1.2)	6 (2.5)	18 (2.5)	5 (2.1)
Withdrawn due to Adverse Events, n (%)	1 (0.4)	1 (0.4)	0 (0.0)	2 (0.3)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons, n (%)	8 (3.3)	2 (0.8)	6 (2.5)	16 (2.2)	5 (2.1)
Demographics	**MMRV_1**	**MMRV_2**	**MMRV_3**	**MMRV**	**MMR+V**
N (Total Vaccinated Cohort)	246	248	238	732	238
Females: Males	112:134	124:124	115:123	351:381	105:133
Mean Age, months (SD)	12.8 (1.98)	12.9 (2.13)	13.0 (2.14)	12.9 (2.08)	12.9 (2.06)
White/Caucasian, n (%)	235 (95.5)	241 (97.2)	225 (94.5)	701 (95.8)	222 (93.3)

Primary Efficacy Results:

Difference between the study vaccine lots in antibody seroconversion rate at post-vaccination blood sample at Day 42 in subjects initially seronegative (ATP Cohort for immunogenicity)

Group 1	**N**	**%**	**Group 2**	**N**	**%**	**Difference in seroconversion rate (Group 2 minus Group 1)**			
						Difference	**%**	**95 % CI**	
								LL*	**UL***
Anti-measles (≥ 150 mIU/mL)									
MMRV_1	226	94.2	**MMRV_2**	228	92.5	**MMRV_2 - MMRV_1**	-1.70	-6.53	3.01
MMRV_1	226	94.2	**MMRV_3**	216	96.8	**MMRV_3 - MMRV_1**	2.51	-1.49	6.75
MMRV_2	228	92.5	**MMRV_3**	216	96.8	**MMRV_3 - MMRV_2**	4.22	0.01	8.77
Anti-mumps (≥ 28 ED50)									
MMRV_1	191	95.8	**MMRV_2**	188	96.8	**MMRV_2 - MMRV_1**	1.00	-3.13	5.26
MMRV_1	191	95.8	**MMRV_3**	179	95.5	**MMRV_3 - MMRV_1**	-0.28	-4.89	4.17
MMRV_2	188	96.8	**MMRV_3**	179	95.5	**MMRV_3 - MMRV_2**	-1.28	-5.77	2.91
Anti-rubella (≥ 4 IU/mL)									
MMRV_1	227	100	**MMRV_2**	226	99.1	**MMRV_2 - MMRV_1**	-0.88	-3.17	0.79
MMRV_1	227	100	**MMRV_3**	214	100	**MMRV_3 - MMRV_1**	0.00	-1.76	1.66
MMRV_2	226	99.1	**MMRV_3**	214	100	**MMRV_3 - MMRV_2**	0.88	-0.89	3.17
Anti-varicella (≥ 1:4)									

MMRV_1	213	94.8	**MMRV_2**	205	95.1	**MMRV_2 - MMRV_1**	0.29	-4.20	4.74
MMRV_1	213	94.8	**MMRV_3**	206	96.6	**MMRV_3 - MMRV_1**	1.77	-2.32	6.04
MMRV_2	205	95.1	**MMRV_3**	206	96.6	**MMRV_3 - MMRV_2**	1.48	-2.59	5.77

N = number of subjects initially seronegative with available results at post-vaccination blood sample at Day 42
% = percentage of subjects with antibody titre ≥ specified cut-off
95% CI = 95% Standardized asymptotic confidence interval; LL = lower limit, UL = upper limit
*The consistency of the 3 different lots was demonstrated as all the pair wise standardized asymptotic 95% CIs for seroconversion rate difference between the lots for each antigen (measles, mumps, rubella and varicella) were within [-10%, 10%].

Primary Efficacy Results:
Seroconversion rates and GMTs for anti-mumps (neutralization assay) antibodies for initially seronegative (antibody titer < 28 ED50 prior to vaccination) subjects (ATP Cohort for immunogenicity)

Group	**Timing**	**N**	**≥ 28 ED50****				**GMT (ED50)**		
			n	**%**	**95% CI**		**value**	**95% CI**	
					LL	**UL**		**LL**	**UL**
MMRV_1	PI(D42)**	191	183	95.8	91.9	98.2	146.5	123.6	173.5
	PII(D84)	182	182	100	98.0	100	568.9	494.7	654.1
MMRV_2	PI(D42)**	188	182	96.8	93.2	98.8	171.6	144.0	204.4
	PII(D84)	187	185	98.9	96.2	99.9	607.4	526.9	700.2
MMRV_3	PI(D42)**	179	171	95.5	91.4	98.1	156.9	132.0	186.6
	PII(D84)	172	171	99.4	96.8	100	592.3	510.6	687.1
MMRV	PI(D42)**	558	536	96.1	94.1*	97.5	157.9	143.0	174.4
	PII(D84)	541	538	99.4	98.4	99.9	589.4	542.9	640.0
MMR+V	PI(D42)**	187	175	93.6	89.1	96.6	124.1	103.6	148.7
	PII(D84)	182	181	99.5	97.0	100	449.0	390.4	516.5

N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with antibody titre ≥ specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PI(D42) = Post-vaccination blood sample at Day 42
PII(D84) = Post-vaccination blood sample at Day 84
*As the LL of the exact 95% CI for mumps seroconversion rate post Dose 1 for the pooled lots was > pre-defined limit of 90% in initially seronegative subjects, a mumps seroconversion rate below 90% for the pooled lots was ruled out
**Primary Outcome/Efficacy variable

Primary Efficacy Results:
Seroconversion rates and GMTs for anti-measles antibodies for initially seronegative (antibody titer < 150 mIU/mL prior to vaccination) subjects (ATP Cohort for immunogenicity)

Group	**Timing**	**N**	**≥ 150 mIU/mL***				**GMT (mIU/mL)**		
			n	**%**	**95% CI**		**Value**	**95% CI**	
					LL	**UL**		**LL**	**UL**
MMRV_1	PI(D42)*	226	213	94.2	90.4	96.9	2564.8	2199.6	2990.6
	PII(D84)	221	218	98.6	96.1	99.7	3632.9	3169.1	4164.6
MMRV_2	PI(D42)*	228	211	92.5	88.3	95.6	2390.2	2031.2	2812.6
	PII(D84)	226	221	97.8	94.9	99.3	3784.8	3309.5	4328.4
MMRV_3	PI(D42)*	216	209	96.8	93.4	98.7	2830.2	2445.7	3275.1
	PII(D84)	210	207	98.6	95.9	99.7	3857.8	3361.0	4427.9
MMRV	PI(D42)*	670	633	94.5	92.5	96.1	2584.7	2364.7	2825.2
	PII(D84)	657	646	98.3	97.0	99.2	3755.9	3473.2	4061.6
MMR+V	PI(D42)*	213	199	93.4	89.2	96.4	1645.4	1399.2	1935.0
	PII(D84)	209	204	97.6	94.5	99.2	2176.0	1878.2	2520.9

N = number of subjects with pre-vaccination results available

n (%) = number (percentage) of subjects with antibody titer ≥ specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PI(D42) = Post-vaccination blood sample at Day 42
PII(D84) = Post-vaccination blood sample at Day 84
*Primary Outcome/Efficacy variable

Primary Efficacy Results:
Seroconversion rates and GMTs for anti-rubella antibodies for initially seronegative (antibody titer < 4 IU/mL prior to vaccination) subjects (ATP Cohort for immunogenicity)

Group	Timing	N	≥ 4 IU/mL*				GMT (IU/mL)		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
MMRV_1	PI(D42)*	227	227	100	98.4	100	67.8	60.9	75.5
	PII(D84)	221	221	100	98.3	100	123.5	112.7	135.3
MMRV_2	PI(D42)*	226	224	99.1	96.8	99.9	58.5	52.4	65.4
	PII(D84)	224	223	99.6	97.5	100	124.6	114.2	136.1
MMRV_3	PI(D42)*	214	214	100	98.3	100	62.8	56.3	70.2
	PII(D84)	208	207	99.5	97.4	100	119.6	108.7	131.6
MMRV	PI(D42)*	667	665	99.7	98.9	100	62.9	59.1	67.0
	PII(D84)	653	651	99.7	98.9	100	122.6	116.4	129.3
MMR+V	PI(D42)*	212	208	98.1	95.2	99.5	83.2	73.4	94.3
	PII(D84)	209	209	100	98.3	100	135.6	124.4	147.9

N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with antibody titer ≥ specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PI(D42) = Post-vaccination blood sample at Day 42
PII(D84) = Post-vaccination blood sample at Day 84
*Primary Outcome/Efficacy variable

Primary Efficacy Results:
Seroconversion rates and GMTs for anti-varicella antibodies for initially seronegative (antibody titer < 1:4 prior to vaccination) subjects (ATP Cohort for immunogenicity)

Group	Timing	N	≥ 1:4*				GMT		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
MMRV_1	PI(D42)*	213	202	94.8	90.9	97.4	65.9	55.0	78.9
	PII(D84)	210	210	100	98.3	100	1742.2	1484.2	2044.9
MMRV_2	PI(D42)*	205	195	95.1	91.2	97.6	91.6	76.5	109.7
	PII(D84)	204	203	99.5	97.3	100	2090.2	1727.8	2528.6
MMRV_3	PI(D42)*	206	199	96.6	93.1	98.6	86.6	73.4	102.2
	PII(D84)	201	200	99.5	97.3	100	1898.4	1572.0	2292.4
MMRV	PI(D42)*	624	596	95.5	93.6	97.0	80.4	72.6	89.0
	PII(D84)	615	613	99.7	98.8	100	1903.3	1716.3	2110.7
MMR+V	PI(D42)*	204	195	95.6	91.8	98.0	84.0	70.3	100.3
	PII(D84)	199	194	97.5	94.2	99.2	80.3	66.0	97.6

N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with antibody titre ≥ specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PI(D42) = Post-vaccination blood sample at Day 42
PII(D84) = Post-vaccination blood sample at Day 84
*Primary Outcome/Efficacy variable

Secondary Outcome Variable (s):
Seroconversion rates and GMTs for anti-mumps (ELISA) antibodies for initially seronegative (antibody titer < 231 U/mL prior to vaccination) subjects (ATP Cohort for immunogenicity)

Group	Timing	N	≥ 231 U/mL				GMT (U/mL)		
			n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL
MMRV_1	PI(D42)	218	203	93.1	88.9	96.1	1013.9	890.5	1154.5
	PII(D84)	223	221	99.1	96.8	99.9	1667.8	1511.9	1839.8
MMRV_2	PI(D42)	225	214	95.1	91.4	97.5	1186.4	1052.8	1337.0
	PII(D84)	225	224	99.6	97.5	100	1840.6	1683.0	2012.9
MMRV_3	PI(D42)	207	196	94.7	90.7	97.3	1083.0	960.5	1221.1
	PII(D84)	208	206	99.0	96.6	99.9	1682.4	1539.1	1839.0
MMRV	PI(D42)	650	613	94.3	92.2	96.0	1093.3	1018.4	1173.7
	PII(D84)	656	651	99.2	98.2	99.8	1729.9	1640.2	1824.5
MMR+V	PI(D42)	207	191	92.3	87.8	95.5	875.6	773.8	990.8
	PII(D84)	208	207	99.5	97.4	100	1397.1	1270.5	1536.4

N = number of subjects with pre-vaccination results available
n (%) = number (percentage) of subjects with antibody titer ≥ specified cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PI(D42) = Post-vaccination blood sample at Day 42
PII(D84) = Post-vaccination blood sample at Day 84

Secondary Outcome Variable (s):
Incidence of solicited local symptoms reported during the 4-day (Day 0-3) post-vaccination period following each dose (Total Vaccinated Cohort)

Symptom	Intensity	MMRV_1				MMRV_2				MMRV_3			
		n	%	95% CI		n	%	95% CI		n	%	95% CI	
				LL	UL			LL	UL			LL	UL
		Dose 1											
		N=246				N=248				N=238			
Pain	Any	17	6.9	4.1	10.8	21	8.5	5.3	12.7	24	10.1	6.6	14.6
	Grade 3	0	0.0	0.0	1.5	0	0.0	0.0	1.5	0	0.0	0.0	1.5
Redness	Any	68	27.6	22.2	33.7	89	35.9	29.9	42.2	75	31.5	25.7	37.8
	> 20 mm	0	0.0	0.0	1.5	1	0.4	0.0	2.2	0	0.0	0.0	1.5
Swelling	Any	29	11.8	8.0	16.5	19	7.7	4.7	11.7	28	11.8	8.0	16.6
	> 20 mm	2	0.8	0.1	2.9	1	0.4	0.0	2.2	2	0.8	0.1	3.0
		Dose 2											
		N=241				N=246				N=238			
Pain	Any	20	8.3	5.1	12.5	23	9.3	6.0	13.7	26	10.9	7.3	15.6
	Grade 3	0	0.0	0.0	1.5	0	0.0	0.0	1.5	0	0.0	0.0	1.5
Redness	Any	68	28.2	22.6	34.4	80	32.5	26.7	38.8	86	36.1	30.0	42.6
	> 20 mm	3	1.2	0.3	3.6	8	3.3	1.4	6.3	6	2.5	0.9	5.4
Swelling	Any	31	12.9	8.9	17.8	32	13.0	9.1	17.9	33	13.9	9.7	18.9
	> 20 mm	1	0.4	0.0	2.3	1	0.4	0.0	2.2	3	1.3	0.3	3.6

Symptom	Intensity	MMRV				MMR+V			
		n	%	95% CI		n	%	95% CI	
				LL	UL			LL	UL
		Dose 1							
		N=732				N=238			
Pain	Any	62	8.5	6.6	10.7	21	8.8	5.5	13.2
	Grade 3	0	0.0	0.0	0.5	0	0.0	0.0	1.5

Redness	Any	232	31.7	28.3	35.2	77	32.4	26.5	38.7
	> 20 mm	1	0.1	0.0	0.8	0	0.0	0.0	1.5
Swelling	Any	76	10.4	8.3	12.8	18	7.6	4.5	11.7
	> 20 mm	5	0.7	0.2	1.6	0	0.0	0.0	1.5
		Dose 2							
		N=725				**N=236**			
Pain	Any	69	9.5	7.5	11.9	16	6.8	3.9	10.8
	Grade 3	0	0.0	0.0	0.5	0	0.0	0.0	1.6
Redness	Any	234	32.3	28.9	35.8	58	24.6	19.2	30.6
	> 20 mm	17	2.3	1.4	3.7	0	0.0	0.0	1.6
Swelling	Any	96	13.2	10.9	15.9	20	8.5	5.3	12.8
	> 20 mm	5	0.7	0.2	1.6	0	0.0	0.0	1.6

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects for whom the symptom was reported at least once
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit
Any = any solicited local symptom irrespective of intensity grade
Grade 3 pain = cried when limb was moved/spontaneously painful

Secondary Outcome Variable (s):
Incidence of solicited general symptoms reported during the 43-day (Day 0-42) post-vaccination period following each dose (Total Vaccinated Cohort)

Symptom	**Intensity/ relationship**	**MMRV_1**				**MMRV_2**				**MMRV_3**			
		n	**%**	**95% CI**		**n**	**%**	**95% CI**		**n**	**%**	**95% CI**	
				LL	**UL**			**LL**	**UL**			**LL**	**UL**
		Dose 1											
		N=246				**N=248**				**N=238**			
Fever (Rectal)	≥ 38.0°C	169	68.7	62.5	74.4	170	68.5	62.4	74.3	162	68.1	61.7	73.9
	> 39.5°C	42	17.1	12.6	22.4	37	14.9	10.7	20.0	37	15.5	11.2	20.8
	Related	105	42.7	36.4	49.1	94	37.9	31.8	44.3	92	38.7	32.4	45.2
Rash	Any	52	21.1	16.2	26.8	47	19.0	14.3	24.4	47	19.7	14.9	25.4
	Grade 3	3	1.2	0.3	3.5	2	0.8	0.1	2.9	5	2.1	0.7	4.8
	Related	10	4.1	2.0	7.3	10	4.0	2.0	7.3	12	5.0	2.6	8.6
Parotid/Salivary Gland swelling	Any	0	0.0	0.0	1.5	1	0.4	0.0	2.2	1	0.4	0.0	2.3
	Grade 3	0	0.0	0.0	1.5	0	0.0	0.0	1.5	0	0.0	0.0	1.5
	Related	0	0.0	0.0	1.5	0	0.0	0.0	1.5	1	0.4	0.0	2.3
Meningism	Any	1	0.4	0.0	2.2	0	0.0	0.0	1.5	1	0.4	0.0	2.3
	Grade 3	1	0.4	0.0	2.2	0	0.0	0.0	1.5	0	0.0	0.0	1.5
	Related	0	0.0	0.0	1.5	0	0.0	0.0	1.5	1	0.4	0.0	2.3
		Dose 2											
		N=241				**N=246**				**N=238**			
Fever (Rectal)	≥ 38.0°C	123	51.0	44.5	57.5	137	55.7	49.2	62.0	113	47.5	41.0	54.0
	> 39.5°C	22	9.1	5.8	13.5	25	10.2	6.7	14.6	23	9.7	6.2	14.1
	Related	58	24.1	18.8	30.0	63	25.6	20.3	31.5	43	18.1	13.4	23.6
Rash	Any	24	10.0	6.5	14.5	37	15.0	10.8	20.1	30	12.6	8.7	17.5
	Grade 3	0	0.0	0.0	1.5	3	1.2	0.3	3.5	1	0.4	0.0	2.3
	Related	3	1.2	0.3	3.6	4	1.6	0.4	4.1	4	1.7	0.5	4.2
Parotid/Salivary Gland swelling	Any	0	0.0	0.0	1.5	0	0.0	0.0	1.5	1	0.4	0.0	2.3
	Grade 3	0	0.0	0.0	1.5	0	0.0	0.0	1.5	0	0.0	0.0	1.5
	Related	0	0.0	0.0	1.5	0	0.0	0.0	1.5	1	0.4	0.0	2.3

Meningism	Any	0	0.0	0.0	1.5	2	0.8	0.1	2.9	0	0.0	0.0	1.5
	Grade 3	0	0.0	0.0	1.5	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Related	0	0.0	0.0	1.5	0	0.0	0.0	1.5	0	0.0	0.0	1.5

Symptom	**Intensity**	**MMRV**				**MMR+V**			
		n	**%**	**95% CI**		**n**	**%**	**95% CI**	
				LL	**UL**			**LL**	**UL**
		Dose 1							
		N=732				**N=238**			
Fever (Rectal)	≥ 38.0°C	501	68.4	64.9	71.8	145	60.9	54.4	67.2
	> 39.5°C	116	15.8	13.3	18.7	36	15.1	10.8	20.3
	Related	291	39.8	36.2	43.4	91	38.2	32.0	44.7
Rash	Any	146	19.9	17.1	23.0	33	13.9	9.7	18.9
	Grade 3	10	1.4	0.7	2.5	2	0.8	0.1	3.0
	Related	32	4.4	3.0	6.1	9	3.8	1.7	7.1
Parotid/Salivary Gland swelling	Any	2	0.3	0.0	1.0	0	0.0	0.0	1.5
	Grade 3	0	0.0	0.0	0.5	0	0.0	0.0	1.5
	Related	1	0.1	0.0	0.8	0	0.0	0.0	1.5
Meningism	Any	2	0.3	0.0	1.0	0	0.0	0.0	1.5
	Grade 3	1	0.1	0.0	0.8	0	0.0	0.0	1.5
	Related	1	0.1	0.0	0.8	0	0.0	0.0	1.5
		Dose 2							
		N=725				**N=236**			
Fever (Rectal)	≥ 38.0°C	373	51.4	47.7	55.1	111	47.0	40.5	53.6
	> 39.5°C	70	9.7	7.6	12.0	22	9.3	5.9	13.8
	Related	164	22.6	19.6	25.8	47	19.9	15.0	25.6
Rash	Any	91	12.6	10.2	15.2	36	15.3	10.9	20.5
	Grade 3	4	0.6	0.2	1.4	5	2.1	0.7	4.9
	Related	11	1.5	0.8	2.7	4	1.7	0.5	4.3
Parotid/Salivary Gland swelling	Any	1	0.1	0.0	0.8	0	0.0	0.0	1.6
	Grade 3	0	0.0	0.0	0.5	0	0.0	0.0	1.6
	Related	1	0.1	0.0	0.8	0	0.0	0.0	1.6
Meningism	Any	2	0.3	0.0	1.0	1	0.4	0.0	2.3
	Grade 3	1	0.1	0.0	0.8	0	0.0	0.0	1.6
	Related	0	0.0	0.0	0.5	0	0.0	0.0	1.6

N = number of subjects with an administered dose
n (%) = number (percentage) of subjects for whom the symptom was reported at least once
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit
Any: any solicited general symptom irrespective of intensity grade or relationship to vaccination
Grade 3 rash: > 150 lesions
Grade 3 parotid/salivary gland swelling: swelling with accompanying general symptoms
Grade 3 meningism: meningism that prevented normal, everyday activities
Related: symptom considered by the investigator to have a causal relationship to vaccination

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

Most Frequent Adverse Events - On-Therapy- (occurring within Day 0-42 following vaccination)	**MMRV_1 N = 246**	**MMRV_2 N = 248**	**MMRV_3 N = 238**	**MMRV N = 732**	**MMR+V N = 238**
Subjects with any AE(s), n (%)	107 (43.5)	116 (46.8)	109 (45.8)	332 (45.4)	103 (43.3)

Subjects with severe AE(s), n (%)	6 (2.4)	4 (1.6)	5 (2.1)	15 (2.0)	3 (1.3)
Subjects with related AE(s), n (%)	5 (2.0)	7 (2.8)	9 (3.8)	21 (2.9)	6 (2.5)
Upper respiratory tract infection	13 (5.3)	21 (8.5)	20 (8.4)	54 (7.4)	24 (10.1)
Otitis media	11 (4.5)	15 (6.0)	11 (4.6)	37 (5.1)	9 (3.8)
Viral infection	11 (4.5)	10 (4.0)	12 (5.0)	33 (4.5)	8 (3.4)
Rhinitis	16 (6.5)	8 (3.2)	8 (3.4)	32 (4.4)	8 (3.4)
Conjunctivitis	12 (4.9)	7 (2.8)	12 (5.0)	31 (4.2)	7 (2.9)
Enteritis	11 (4.5)	8 (3.2)	7 (2.9)	26 (3.6)	10 (4.2)
Cough	10 (4.1)	12 (4.8)	4 (1.7)	26 (3.6)	5 (2.1)
Bronchitis	6 (2.4)	8 (3.2)	9 (3.8)	23 (3.1)	6 (2.5)
Gastroenteritis	8 (3.3)	9 (3.6)	5 (2.1)	22 (3.0)	4 (1.7)
Safety Results: Number (%) of subjects with unsolicited adverse events after the second dose (Total Vaccinated Cohort)					
Most Frequent Adverse Events - On-Therapy- (occurring within Day 0-42 following vaccination)	**MMRV_1 N = 241**	**MMRV_2 N = 246**	**MMRV_3 N = 238**	**MMRV N = 725**	**MMR+V N = 236**
Subjects with any AE(s), n (%)	95 (39.4)	112 (45.5)	91 (38.2)	298 (41.1)	73 (30.9)
Subjects with severe AE(s), n (%)	4 (1.7)	1 (0.4)	6 (2.5)	11 (1.5)	1 (0.4)
Subjects with related AE(s), n (%)	1 (0.4)	5 (2.0)	2 (0.8)	8 (1.1)	4 (1.7)
Upper respiratory tract infection	19 (7.9)	22 (8.9)	19 (8.0)	60 (8.3)	15 (6.4)
Rhinitis	15 (6.2)	17 (6.9)	11 (4.6)	43 (5.9)	7 (3.0)
Bronchitis	6 (2.5)	12 (4.9)	11 (4.6)	29 (4.0)	7 (3.0)
Gastroenteritis	8 (3.3)	7 (2.8)	9 (3.8)	24 (3.3)	5 (2.1)
Viral infection	8 (3.3)	12 (4.9)	2 (0.8)	22 (3.0)	8 (3.4)
Cough	8 (3.3)	6 (2.4)	9 (3.8)	23 (3.2)	5 (2.1)
Otitis media	7 (2.9)	9 (3.7)	7 (2.9)	23 (3.2)	4 (1.7)
Teething	9 (3.7)	8 (3.3)	4 (1.7)	21 (2.9)	5 (2.1)
Conjunctivitis	6 (2.5)	9 (3.7)	2 (0.8)	17 (2.3)	3 (1.3)
Enteritis	3 (1.2)	4 (1.6)	9 (3.8)	16 (2.2)	3 (1.3)
Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) (Total Vaccinated Cohort)					
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]					
All SAEs	**MMRV_1 N = 246**	**MMRV_2 N = 248**	**MMRV_3 N = 238**	**MMRV N = 732**	**MMR+V N = 238**
Subjects with any SAE(s), n (%) [n related]	2 (0.8) [0]	4 (1.6) [0]	4 (1.7) [1]	10 (1.4) [1]	4 (1.7) [0]
Febrile convulsion	1 (0.4) [0]	1 (0.4) [0]	1 (0.4) [1]	3 (0.4) [1]	0 (0.0) [0]
Bronchitis	0 (0.0) [0]	1 (0.4) [0]	1 (0.4) [0]	2 (0.3) [0]	0 (0.0) [0]
Viral infection	0 (0.0) [0]	1 (0.4) [0]	0 (0.0) [0]	1 (0.1) [0]	1 (0.4) [0]
Acute tonsillitis	0 (0.0) [0]	0 (0.0) [0]	1 (0.4) [1]	1 (0.1) [1]	0 (0.0) [0]
Animal bite	0 (0.0) [0]	0 (0.0) [0]	1 (0.4) [0]	1 (0.1) [0]	0 (0.0) [0]
Cellulitis orbital	0 (0.0) [0]	1 (0.4) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Contusion	0 (0.0) [0]	0 (0.0) [0]	1 (0.4) [0]	1 (0.1) [0]	0 (0.0) [0]
Dermatitis diaper	0 (0.0) [0]	1 (0.4) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Exanthema subitum	0 (0.0) [0]	1 (0.4) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Hepatic trauma	0 (0.0) [0]	0 (0.0) [0]	1 (0.4) [0]	1 (0.1) [0]	0 (0.0) [0]
Human herpesvirus 6 infection	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Laryngotracheo bronchitis	1 (0.4) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Meningitis meningococcal	0 (0.0) [0]	1 (0.4) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Otitis media	0 (0.0) [0]	1 (0.4) [0]	0 (0.0) [0]	1 (0.1) [0]	0 (0.0) [0]
Enteritis	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.4) [0]

Gastroenteritis	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.4) [0]
Head injury	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.4) [0]
Upper respiratory tract infection	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	1 (0.4) [0]
Fatal SAEs	**MMRV_1 N = 246**	**MMRV_2 N = 248**	**MMRV_3 N = 238**	**MMRV N = 732**	**MMR+V N = 238**
Subjects with fatal SAE(s), n (%) [n related]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]	0 (0.0) [0]

Conclusion: The primary objective was as the consistency of the 3 different lots of vaccine was demonstrated in terms of measles, mumps, rubella and varicella seroconversion after the first dose. For the remaining immuno results and all safety results, please also refer to the publications below.

Publications:

Schuster V et al. Immunogenicity of a Refrigerator-Stable Tetravalent MMRV Vaccine after One and Two Doses. Presented at the 24th Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), Basel, Switzerland, 3-5 May 2006.

Schuster V et al. Tolerability of a Refrigerator-Stable Tetravalent MMRV vaccine after One and Two Doses. Presented at the 12th International Congress on Infectious Diseases (ICID), Lisbon, Portugal, 15-18 June 2006.

Schuster V et al. (2008) Immunogenicity and Safety Assessments After One and Two Doses of a Refrigerator-Stable Tetravalent Measles-Mumps-Rubella-Varicella Vaccine in Healthy Children During the Second Year of Life. Pediatr Infect Dis J. 27(8):724-730.

Sohita D et al. (2008) Live Attenuated Measles, Mumps, Rubella, and Varicella Zoster Virus Vaccine (Priorix-Tetra). Pediatric Drugs. 10 (5):337-347.

Date updated: 27 Mar 2009