This report may include approved and non-approved uses, formulations, or treatment regimens. The results reported may not reflect the overall profile of a product. Before prescribing any product mentioned in this report, healthcare professionals should consult local prescribing information for the product approved in their country.

2. Synopsis

MERCK SHARP & DOHME CORP., A SUBSIDIARY OF MERCK & CO., INC. V114 pneumococcal conj vaccine (CRM197), Sterile Suspension for Intramuscular Injection The prevention of pneumococcal disease caused by *S. pneumoniae* due to capsular serotypes included in the vaccine (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F) in infants and toddlers	**CLINICAL STUDY REPORT SYNOPSIS**

PROTOCOL TITLE/NO.: A Multicenter, Double-Blind Study of the Safety, Tolerability, and Immunogenicity of Pneumococcal Conjugate Vaccine (V114) Compared to Prevnar™ in Healthy Adults and Toddlers #001

INVESTIGATOR(S)/STUDY CENTER(S): Multicenter (13) in the United States and (3) in Finland

PRIMARY THERAPY PERIOD: 25-Sept-2009 to 15-Mar-2010 **CLINICAL PHASE:** I

DURATION OF TREATMENT: Subjects received 1 dose of blinded study vaccine on Day 1

OBJECTIVE(S):

Primary: **Safety Adult Stage:** To evaluate the safety profile of a single dose of the aluminum-adjuvanted formulation of V114 pneumococcal conjugate vaccine versus Prevnar™ in healthy adults. **Safety Toddler Stage:** To evaluate the safety profile of a single booster dose of the aluminum-adjuvanted, and the nonadjuvanted formulation of V114 versus Prevnar™ administered at 12-15 months of age in healthy toddlers.

Secondary: **Immunogenicity:** To describe the immunogenicity response to the serotypes contained in V114 in both adults and toddlers as measured by the MSD electrochemiluminescence (ECL) assay for the measurement of serotype-specific pneumococcal capsular polysaccharide IgG antibodies. Sera were also assayed by a multiplex OPA for opsonophagocytic killing activity. The main immunogenicity measurement is the pneumococcal capsular polysaccharide IgG concentration as measured by the pneumococcal electrochemiluminescence (Pn ECL) assay, and corresponding to the 0.35 μg/mL level as measured by the internationally accepted ELISA.

HYPOTHESIS:

This is a descriptive study; therefore, there are no hypotheses.

STUDY DESIGN: A multicenter, randomized, double-blind (with in-house blinding procedures), active control trial conducted in the US and Finland to evaluate the safety, tolerability, and immunogenicity of 15-valent pneumococcal conjugate vaccine (V114) compared to Prevnar™ in healthy adults and toddlers. The safety of a single dose administration of the study vaccines was first evaluated in healthy adults. Adults were randomly assigned to 1 of 2 treatment arms: (1) Merck investigational V114, aluminum-adjuvanted or (2) Prevnar™ control arm. After completion of a safety review of the adult stage data by an external Data Monitoring Committee (eDMC), toddlers (documented to have completed a 3-dose infant series of Prevnar™), were randomized to receive a booster dose of either (1) Merck investigational V114, aluminum-adjuvanted, or (2) Merck investigational V114, nonadjuvanted, or (3) Prevnar™ used as control. During the toddler stage, study vaccine was allowed to be administered concomitantly with other licensed routine pediatric vaccines normally administered at 12-15 months of age.

SUBJECT/PATIENT DISPOSITION: Adults

	V114 adjuvanted	Prevnar™	Total
SCREENING FAILURES:	0	0	0
RANDOMIZED:			
Male (20-45 yrs.)	17	14	31
Female (20-45 yrs.)	13	16	29
COMPLETED:	30	29	59
DISCONTINUED:	0	1	1
Clinical adverse experience	0	0	0
Laboratory adverse experience	0	0	0
Lost to follow-up	0	1	1

SUBJECT/PATIENT DISPOSITION: Toddlers

	V114 adjuvanted	V114 nonadjuvanted	Prevnar™	Total
SCREENING FAILURES:	0	0	0	0
RANDOMIZED:				
Male (12-15 mos.)	12	14	11	37
Female (12-15 mos.)	21	15	17	53
COMPLETED:	33	28	28	89
DISCONTINUED:	0	1	0	1
Clinical adverse experience	0	0	0	0
Laboratory adverse experience	0	0	0	0
Lost to follow-up	0	1	0	1

DOSAGE/FORMULATION NOS.: A single 0.5 mL intramuscular dose of study vaccine (aluminum-adjuvanted V114 or Prevnar™) was administered to adult subjects. A 0.5 mL intramuscular dose of study vaccine (aluminum-adjuvanted V114, nonadjuvanted V114, or Prevnar™) was administered to healthy toddlers at 12-15 months of age who had completed a full 3-dose infant series of Prevnar™ at 2, 4, and 6 months of age.

Clinical Supplies Used in V114-001-01

Vaccine	Market Lot Number	Fill Number	Bulk Number(s)	Potency (Polysaccharide content per dose)
V114 adjuvanted	[redacted]			See footnote*
V114 nonadjuvanted				See footnote ^
Prevnar				See footnote #
Prevnar				See footnote #
Prevnar				See footnote #
Prevnar				See footnote #

*V114 contains 2µg of 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F and 4 µg of 6B; 32µg of CRM_{197} and 125µg of elemental aluminum as aluminum phosphate (MAPA) per 0.5 mL dose.
^ V114 nonadjuvanted contains 2µg of 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F and 4µg of 6B; 32µg of CRM_{197} per 0.5 mL dose.
#Prevnar contains 2µg of 4, 9V, 14, 18C, 19F and 23F and 4µg of 6B; 20µg of CRM_{197} and 125µg of aluminum per 0.5mL dose.

DIAGNOSIS/INCLUSION CRITERIA: Afebrile healthy adult subjects ≥18 to 45 years of age. Afebrile healthy toddlers 12-15 months of age documented to have completed a full 3-dose infant series of Prevnar™ at 2, 4, and 6 months of age.

EVALUATION CRITERIA:

Immunogenicity: Serotype-specific IgG concentrations were measured using the Meso-Scale Discovery (MSD) electrochemiluminescence (ECL) assay on sera collected prior to vaccination and 30 days postvaccination (MSD is a trademark of Meso Scale Discovery, a division of Meso Scale Diagnostics, LLC., Gaithersburg, MD, U.S.A.). A multiplex OPA assay was used to measure OPA activity in the pre- and post vaccination sera. The percentage of subjects with postvaccination serotype-specific IgG concentrations corresponding to a level of ≥0.35 μg/mL in the WHO ELISA was evaluated. Other endpoints of interest were the geometric mean concentrations of IgG, the percentage of subjects with opsonophagocytic killing activity (OPA) as defined by functional antibacterial OPA titer ≥1:8 and the geometric mean OPA titers for the serotypes contained in the V114 vaccine. **Safety:** Adverse experiences were collected using a validated vaccine report card (VRC). All adverse experiences (AEs) were graded for severity. **Adult and Toddler Stages:** 1) Study subjects were observed for 30 minutes postvaccination for any immediate adverse experiences. 2) Solicited injection site adverse experiences (redness, swelling, nodules, and pain/tenderness) and solicited systemic adverse experiences (muscle pain, joint pain, and tiredness) were collected Day 1 to Day 14 after vaccination. 3) Any other systemic or injection site adverse experiences were collected Day 1 to Day 14 after vaccination. 4) Serious adverse experiences from the time the consent form was signed through completion of the subject's participation in the study at Day 30 after receipt of study vaccine. 5) Body temperature was measured during Day 1 to Day 7 after vaccination. If fever was suspected, body temperature was also measured during Day 8 to Day 14. **Adults Only:** 1) CBC with differential including platelets, serum creatinine, ALK, ALT, bilirubin, and urinalysis was performed at Day 1 and Day 14; 2) Severity of AEs and safety laboratory abnormalities were assessed according to a toxicity grading scale as mild (Grade I), moderate (Grade II), severe (Grade III), and potentially life threatening (Grade IV).

STATISTICAL PLANNING AND ANALYSIS: Immunogenicity Analyses: Because there are no immunogenicity hypotheses for this study, only observational comparisons by treatment group were made within both the adult and toddler cohorts. For the summary analysis of the main endpoint, the percentage of subjects who achieved an IgG concentration corresponding to a threshold level of ≥ 0.35 μg/mL in the WHO ELISA were calculated along with 95% confidence intervals per treatment group for each serotype contained in V114. The confidence intervals were calculated according to the Clopper-Pearson method. Other summary analyses included IgG geometric mean concentrations and OPA geometric mean titers for each vaccine serotype. The GMCs and GMTs were calculated along with the 95% confidence intervals. Point estimates of GMCs and GMTs are the exponentiated estimates of the mean log concentrations. The confidence intervals for GMCs and GMTs are the exponentiated confidence intervals for the mean log concentrations, based on 1-sample t-distributions. The percentage of subjects with OPA titer ≥1:8 were summarized according to the same methods described above for the main endpoint. **Safety Analyses:** There are no safety hypotheses for this study. The summary analysis of safety results followed a tiered approach. The tiers differ with respect to the analyses that were performed. There were no safety parameters or adverse experiences of special interest that were identified as a priori and constituted "Tier 1" safety endpoints. Safety parameters were considered Tier 2 or Tier 3. Tier 2 parameters were assessed via point estimates with 95% confidence intervals provided for between-group (V114 versus Prevnar™) comparisons using the Miettinen and Nurminen method (1985); only point estimates by treatment group were provided for Tier 3 safety parameters. Adverse experiences (specific terms as well as system organ class terms) were classified as belonging to "Tier 2" or "Tier 3", based on the number of events observed. Membership in Tier 2 required that at least 4 subjects in any treatment group exhibited the event; all other adverse experiences belonged to Tier 3. For this protocol, the broad clinical and laboratory AE categories consisting of the percentage of subjects with any AE, a vaccine related AE, a serious AE, an AE which is both vaccine-related and serious, and who discontinued due to an AE were also considered Tier 2 endpoints.

RESULTS: Immunogenicity: Among adults, a single dose of aluminum-adjuvanted V114 induced IgG antibody response to all serotypes included in the vaccine. The proportions of subjects achieving serotype-specific antibody concentration by pneumococcal ECL (Pn ECL) assay corresponding to the WHO ELISA IgG threshold value of ≥ 0.35 µg/mL were comparable between recipients of V114 and Prevnar™ for all serotypes in common, based on overlapping 95% confidence intervals. In addition, the IgG geometric mean concentrations (GMCs) were comparable for all serotypes in common, based on overlapping 95% confidence intervals. Among toddlers, a booster dose of aluminum-adjuvanted V114 or nonadjuvanted V114 induced IgG antibody response to all serotypes included in the vaccine; of note, data related to serotype 22F were considered experimental due to failure of assay validity criteria associated with the performance of the positive control sera. The proportions of subjects achieving serotype-specific antibody concentration by pneumococcal ECL (Pn ECL) assay corresponding to the WHO ELISA IgG threshold value of ≥ 0.35 µg/mL were comparable between recipients of either formulation of V114 and Prevnar™ for all serotypes in common, based on overlapping 95% confidence intervals. In addition, the IgG geometric mean concentrations (GMCs) were generally comparable for the serotypes in common, as the analysis demonstrated overlapping 95% confidence intervals for all comparisons except for one, where the aluminum-adjuvanted GMC was lower relative to Prevnar™ for serotype 19F.

Additionally, functional activity based on the opsonophagocytic killing activity (OPA) assay was also demonstrated for recipients of V114, among both adults and toddlers. The proportions of subjects achieving the internationally accepted OPA titer ≥1:8, and the geometric mean titers were comparable between recipients of V114 and Prevnar™ for all serotypes in common.

Summary of IgG Antibody Responses to the Serotypes in Common with Prevnar by Treatment Group Per Protocol Population Adult Cohort

Pneumococcal Serotype	Time Point	Endpoint	V114 Aluminum Adjuvanted			Prevnar		
			n	Observed response	95% CI	n	Observed response	95% CI
4	Predose	%>=level†	26	30.8% (8/26)	(14.3%, 51.8%)	25	32.0% (8/25)	(14.9%, 53.5%)
		GMC µg/mL	26	0.3	(0.2, 0.5)	25	0.4	(0.2, 0.5)
	Postdose	%>=level†	26	100.0% (26/26)	(86.8%, 100.0%)	23	100.0% (23/23)	(85.2%, 100.0%)
		GMC µg/mL	26	4.2	(2.6, 6.9)	23	3.4	(2.3, 5.0)
6B	Predose	%>=level†	26	46.2% (12/26)	(26.6%, 66.6%)	25	44.0% (11/25)	(24.4%, 65.1%)
		GMC µg/mL	26	0.7	(0.5, 1.1)	25	0.7	(0.4, 1.1)
	Postdose	%>=level†	26	96.2% (25/26)	(80.4%, 99.9%)	23	87.0% (20/23)	(66.4%, 97.2%)
		GMC µg/mL	26	20.1	(10.9, 37.2)	23	5.9	(2.5, 13.8)
9V	Predose	%>=level†	26	46.2% (12/26)	(26.6%, 66.6%)	25	40.0% (10/25)	(21.1%, 61.3%)
		GMC µg/mL	26	0.6	(0.4, 0.9)	25	0.7	(0.4, 1.0)
	Postdose	%>=level†	26	100.0% (26/26)	(86.8%, 100.0%)	23	95.7% (22/23)	(78.1%, 99.9%)
		GMC µg/mL	26	7.9	(4.8, 13.2)	23	7.4	(4.4, 12.4)
14	Predose	%>=level†	26	73.1% (19/26)	(52.2%, 88.4%)	25	72.0% (18/25)	(50.6%, 87.9%)
		GMC µg/mL	26	1.8	(1.0, 3.3)	25	0.9	(0.5, 1.7)
	Postdose	%>=level†	26	100.0% (26/26)	(86.8%, 100.0%)	23	95.7% (22/23)	(78.1%, 99.9%)
		GMC µg/mL	26	25.8	(15.8, 42.0)	23	12.5	(6.7, 23.4)
18C	Predose	%>=level†	26	57.7% (15/26)	(36.9%, 76.6%)	25	36.0% (9/25)	(18.0%, 57.5%)
		GMC µg/mL	26	0.8	(0.5, 1.2)	25	0.6	(0.4, 0.8)
	Postdose	%>=level†	26	100.0% (26/26)	(86.8%, 100.0%)	23	95.7% (22/23)	(78.1%, 99.9%)
		GMC µg/mL	26	14.7	(8.7, 24.8)	23	8.6	(4.5, 16.7)
19F	Predose	%>=level†	26	92.3% (24/26)	(74.9%, 99.1%)	25	84.0% (21/25)	(63.9%, 95.5%)
		GMC µg/mL	26	1.6	(1.1, 2.3)	25	1.4	(0.9, 2.3)
	Postdose	%>=level†	26	100.0% (26/26)	(86.8%, 100.0%)	23	100.0% (23/23)	(85.2%, 100.0%)
		GMC µg/mL	26	12.1	(7.1, 20.6)	23	7.5	(4.5, 12.7)
23F	Predose	%>=level†	26	53.8% (14/26)	(33.4%, 73.4%)	25	40.0% (10/25)	(21.1%, 61.3%)
		GMC µg/mL	26	0.9	(0.5, 1.5)	25	0.5	(0.3, 0.9)
	Postdose	%>=level†	26	96.2% (25/26)	(80.4%, 99.9%)	23	100.0% (23/23)	(85.2%, 100.0%)
		GMC µg/mL	26	11.2	(5.8, 21.7)	23	14.2	(7.8, 25.9)

†Serotype-specific IgG antibody concentration measured by the ECL assay corresponding to a level of 0.35 µg/mL in the WHO ELISA. This concentration is 0.4 µg/mL for Serotype 4, 0.69 µg/mL for Serotype 6B, 0.66 µg/mL for Serotype 9V, 0.5 µg/mL for Serotype 14 , 0.71 µg/mL for Serotype 18C, 0.41 µg/mL for Serotype 19F, and 0.61 µg/mL for Serotype 23F.
n = Number of subjects contributing to the analysis.
GMC = Geometric mean concentration.
CI = Confidence interval.

Summary of IgG Antibody Responses to the Serotypes not in Common with Prevnar by Treatment Group Per Protocol Population Adult Cohort

Pneumococcal Serotype	Time Point	Endpoint	V114 Aluminum Adjuvanted			Prevnar		
			n	Observed response	95% CI	n	Observed response	95% CI
1	Predose	%>=level†	26	42.3% (11/26)	(23.4%, 63.1%)	25	36.0% (9/25)	(18.0%, 57.5%)
		GMC µg/mL	26	0.6	(0.5, 0.7)	25	0.6	(0.4, 0.9)
	Postdose	%>=level†	26	96.2% (25/26)	(80.4%, 99.9%)	24	41.7% (10/24)	(22.1%, 63.4%)
		GMC µg/mL	26	7.9	(4.5, 13.8)	24	0.7	(0.5, 1.0)
3	Predose	%>=level†	26	46.2% (12/26)	(26.6%, 66.6%)	25	68.0% (17/25)	(46.5%, 85.1%)
		GMC µg/mL	26	0.9	(0.6, 1.3)	25	0.8	(0.6, 1.2)
	Postdose	%>=level†	26	100.0% (26/26)	(86.8%, 100.0%)	24	83.3% (20/24)	(62.6%, 95.3%)
		GMC µg/mL	26	2.9	(2.0, 4.3)	24	1.1	(0.8, 1.5)
5	Predose	%>=level†	26	100.0% (26/26)	(86.8%, 100.0%)	25	92.0% (23/25)	(74.0%, 99.0%)
		GMC µg/mL	26	1.6	(1.3, 2.1)	25	1.6	(1.2, 2.1)
	Postdose	%>=level†	26	100.0% (26/26)	(86.8%, 100.0%)	24	95.8% (23/24)	(78.9%, 99.9%)
		GMC µg/mL	26	15.1	(8.3, 27.5)	24	1.8	(1.4, 2.4)
6A	Predose	%>=level†	26	61.5% (16/26)	(40.6%, 79.8%)	25	60.0% (15/25)	(38.7%, 78.9%)
		GMC µg/mL	26	0.9	(0.6, 1.4)	25	0.9	(0.6, 1.3)
	Postdose	%>=level†	26	96.2% (25/26)	(80.4%, 99.9%)	23	87.0% (20/23)	(66.4%, 97.2%)
		GMC µg/mL	26	12.4	(6.3, 24.6)	23	4.0	(1.9, 8.6)
7F	Predose	%>=level†	26	53.8% (14/26)	(33.4%, 73.4%)	25	44.0% (11/25)	(24.4%, 65.1%)
		GMC µg/mL	26	0.6	(0.5, 0.8)	25	0.6	(0.4, 0.9)
	Postdose	%>=level†	26	96.2% (25/26)	(80.4%, 99.9%)	24	50.0% (12/24)	(29.1%, 70.9%)
		GMC µg/mL	26	6.8	(3.9, 12.0)	24	0.7	(0.5, 1.0)
19A	Predose	%>=level†	26	92.3% (24/26)	(74.9%, 99.1%)	25	96.0% (24/25)	(79.6%, 99.9%)
		GMC µg/mL	26	2.5	(1.6, 4.0)	25	1.9	(1.3, 2.8)
	Postdose	%>=level†	26	100.0% (26/26)	(86.8%, 100.0%)	24	100.0% (24/24)	(85.8%, 100.0%)
		GMC µg/mL	26	19.1	(12.7, 28.8)	24	5.8	(3.5, 9.5)
22F	Predose	%>=level†	26	57.7% (15/26)	(36.9%, 76.6%)	25	40.0% (10/25)	(21.1%, 61.3%)
		GMC µg/mL	26	0.9	(0.6, 1.4)	25	0.6	(0.4, 0.8)
	Postdose	%>=level†	26	96.2% (25/26)	(80.4%, 99.9%)	24	45.8% (11/24)	(25.6%, 67.2%)
		GMC µg/mL	26	5.9	(3.8, 8.9)	24	0.7	(0.5, 1.0)
33F	Predose	%>=level†	26	65.4% (17/26)	(44.3%, 82.8%)	25	68.0% (17/25)	(46.5%, 85.1%)
		GMC µg/mL	26	1.5	(0.9, 2.6)	25	1.0	(0.6, 1.7)
	Postdose	%>=level†	26	96.2% (25/26)	(80.4%, 99.9%)	24	62.5% (15/24)	(40.6%, 81.2%)
		GMC µg/mL	26	8.2	(4.8, 14.1)	24	1.1	(0.6, 2.1)

†Serotype-specific IgG antibody concentration measured by the ECL assay corresponding to a level of 0.35 µg/mL in the WHO ELISA. This concentration is 0.59 µg/mL for all serotypes.
n = Number of subjects contributing to the analysis.
GMC = Geometric mean concentration.
CI = Confidence interval.

Summary of IgG Antibody Responses to the Serotypes in Common with Prevnar by Treatment Group Per Protocol Population Toddler Cohort

Pneumococcal Serotype	Time Point	Endpoint	V114 Aluminum Adjuvanted			V114 Nonadjuvanted			Prevnar		
			n	Observed response	95% CI	n	Observed response	95% CI	n	Observed response	95% CI
4	Predose	%>=level†	30	33.3% (10/30)	(17.3%, 52.8%)	24	58.3% (14/24)	(36.6%, 77.9%)	24	33.3% (8/24)	(15.6%, 55.3%)
		GMC µg/mL	30	0.3	(0.2, 0.4)	24	0.4	(0.3, 0.5)	24	0.3	(0.3, 0.4)
	Postdose	%>=level†	30	93.3% (28/30)	(77.9%, 99.2%)	23	100.0% (23/23)	(85.2%, 100.0%)	22	100.0% (22/22)	(84.6%, 100.0%)
		GMC µg/mL	30	1.5	(1.0, 2.2)	23	2.5	(1.7, 3.9)	22	2.8	(1.9, 4.0)
6B	Predose	%>=level†	30	30.0% (9/30)	(14.7%, 49.4%)	24	58.3% (14/24)	(36.6%, 77.9%)	24	50.0% (12/24)	(29.1%, 70.9%)
		GMC µg/mL	30	0.5	(0.4, 0.8)	24	0.7	(0.4, 1.2)	24	0.6	(0.4, 0.9)
	Postdose	%>=level†	30	100.0% (30/30)	(88.4%, 100.0%)	23	95.7% (22/23)	(78.1%, 99.9%)	22	95.5% (21/22)	(77.2%, 99.9%)
		GMC µg/mL	30	7.1	(4.8, 10.6)	23	8.2	(5.2, 12.9)	22	7.0	(4.5, 10.9)
9V	Predose	%>=level†	30	36.7% (11/30)	(19.9%, 56.1%)	24	66.7% (16/24)	(44.7%, 84.4%)	24	58.3% (14/24)	(36.6%, 77.9%)
		GMC µg/mL	30	0.6	(0.4, 0.8)	24	0.8	(0.6, 1.2)	24	0.8	(0.5, 1.1)
	Postdose	%>=level†	30	100.0% (30/30)	(88.4%, 100.0%)	23	100.0% (23/23)	(85.2%, 100.0%)	22	100.0% (22/22)	(84.6%, 100.0%)
		GMC µg/mL	30	3.3	(2.4, 4.6)	23	4.7	(3.3, 6.8)	22	5.9	(3.6, 9.9)
14	Predose	%>=level†	30	90.0% (27/30)	(73.5%, 97.9%)	24	91.7% (22/24)	(73.0%, 99.0%)	24	91.7% (22/24)	(73.0%, 99.0%)
		GMC µg/mL	30	1.7	(1.2, 2.5)	24	2.3	(1.4, 3.9)	24	1.8	(1.2, 2.5)
	Postdose	%>=level†	30	100.0% (30/30)	(88.4%, 100.0%)	23	100.0% (23/23)	(85.2%, 100.0%)	22	100.0% (22/22)	(84.6%, 100.0%)
		GMC µg/mL	30	9.4	(6.0, 14.7)	23	10.0	(7.1, 14.1)	22	10.8	(6.1, 18.8)
18C	Predose	%>=level†	30	16.7% (5/30)	(5.6%, 34.7%)	24	41.7% (10/24)	(22.1%, 63.4%)	24	12.5% (3/24)	(2.7%, 32.4%)
		GMC µg/mL	30	0.4	(0.3, 0.5)	24	0.6	(0.4, 0.8)	24	0.4	(0.3, 0.6)
	Postdose	%>=level†	30	86.7% (26/30)	(69.3%, 96.2%)	23	95.7% (22/23)	(78.1%, 99.9%)	22	100.0% (22/22)	(84.6%, 100.0%)
		GMC µg/mL	30	2.1	(1.4, 3.1)	23	2.7	(1.8, 4.0)	22	3.9	(2.7, 5.8)
19F	Predose	%>=level†	30	56.7% (17/30)	(37.4%, 74.5%)	24	70.8% (17/24)	(48.9%, 87.4%)	24	58.3% (14/24)	(36.6%, 77.9%)
		GMC µg/mL	30	0.5	(0.4, 0.7)	24	0.6	(0.5, 0.9)	24	0.6	(0.4, 0.9)
	Postdose	%>=level†	30	96.7% (29/30)	(82.8%, 99.9%)	23	100.0% (23/23)	(85.2%, 100.0%)	22	100.0% (22/22)	(84.6%, 100.0%)
		GMC µg/mL	30	1.9	(1.4, 2.7)	23	2.7	(1.9, 3.7)	22	4.2	(2.8, 6.1)

Summary of IgG Antibody Responses to the Serotypes in Common with Prevnar by Treatment Group Per Protocol Population Toddler Cohort

Pneumococcal Serotype	Time Point	Endpoint	V114 Aluminum Adjuvanted			V114 Nonadjuvanted			Prevnar		
			n	Observed response	95% CI	n	Observed response	95% CI	n	Observed response	95% CI
23F	Predose	%>=level†	30	43.3% (13/30)	(25.5%, 62.6%)	24	50.0% (12/24)	(29.1%, 70.9%)	24	37.5% (9/24)	(18.8%, 59.4%)
		GMC µg/mL	30	0.6	(0.4, 0.8)	24	0.6	(0.3, 1.1)	24	0.5	(0.4, 0.7)
	Postdose	%>=level†	30	100.0% (30/30)	(88.4%, 100.0%)	23	95.7% (22/23)	(78.1%, 99.9%)	22	100.0% (22/22)	(84.6%, 100.0%)
		GMC µg/mL	30	4.3	(3.1, 6.0)	23	4.3	(3.0, 6.2)	22	7.1	(4.6, 10.9)

†Serotype-specific IgG antibody concentration measured by the ECL assay corresponding to a level of 0.35 µg/mL in the WHO ELISA. This concentration is 0.4 µg/mL for Serotype 4, 0.69 µg/mL for Serotype 6B, 0.66 µg/mL for Serotype 9V, 0.5 µg/mL for Serotype 14 , 0.71 µg/mL for Serotype 18C, 0.41 µg/mL for Serotype 19F, and 0.61 µg/mL for Serotype 23F.
n = Number of subjects contributing to the analysis.
GMC = Geometric mean concentration.
CI = Confidence interval.

Summary of IgG Antibody Responses to the Serotypes not in Common with Prevnar by Treatment Group Per Protocol Population Toddler Cohort

Pneumococcal Serotype	Time Point	Endpoint	V114 Aluminum Adjuvanted			V114 Nonadjuvanted			Prevnar		
			n	Observed response	95% CI	n	Observed response	95% CI	n	Observed response	95% CI
1	Predose	%>=level†	30	3.3% (1/30)	(0.1%, 17.2%)	24	4.2% (1/24)	(0.1%, 21.1%)	24	0.0% (0/24)	(0.0%, 14.2%)
		GMC µg/mL	30	0.0	(0.0, 0.1)	24	0.0	(0.0, 0.1)	24	0.0	(0.0, 0.1)
	Postdose	%>=level†	30	100.0% (30/30)	(88.4%, 100.0%)	23	95.7% (22/23)	(78.1%, 99.9%)	22	0.0% (0/22)	(0.0%, 15.4%)
		GMC µg/mL	30	3.0	(2.3, 4.1)	23	4.3	(2.8, 6.6)	22	0.1	(0.0, 0.1)
3	Predose	%>=level†	30	3.3% (1/30)	(0.1%, 17.2%)	24	8.3% (2/24)	(1.0%, 27.0%)	24	4.2% (1/24)	(0.1%, 21.1%)
		GMC µg/mL	30	0.1	(0.1, 0.2)	24	0.2	(0.1, 0.4)	24	0.1	(0.1, 0.2)
	Postdose	%>=level†	30	93.3% (28/30)	(77.9%, 99.2%)	23	95.7% (22/23)	(78.1%, 99.9%)	22	18.2% (4/22)	(5.2%, 40.3%)
		GMC µg/mL	30	2.2	(1.6, 3.0)	23	2.5	(1.7, 3.6)	22	0.4	(0.3, 0.5)
5	Predose	%>=level†	30	50.0% (15/30)	(31.3%, 68.7%)	24	58.3% (14/24)	(36.6%, 77.9%)	24	54.2% (13/24)	(32.8%, 74.4%)
		GMC µg/mL	30	0.5	(0.3, 0.6)	24	0.5	(0.3, 0.9)	24	0.5	(0.3, 0.8)
	Postdose	%>=level†	30	90.0% (27/30)	(73.5%, 97.9%)	23	95.7% (22/23)	(78.1%, 99.9%)	22	68.2% (15/22)	(45.1%, 86.1%)
		GMC µg/mL	30	1.8	(1.3, 2.5)	23	2.5	(1.8, 3.5)	22	0.7	(0.4, 1.0)
6A	Predose	%>=level†	30	23.3% (7/30)	(9.9%, 42.3%)	24	25.0% (6/24)	(9.8%, 46.7%)	24	25.0% (6/24)	(9.8%, 46.7%)
		GMC µg/mL	30	0.3	(0.2, 0.5)	24	0.3	(0.2, 0.5)	24	0.3	(0.2, 0.5)
	Postdose	%>=level†	30	96.7% (29/30)	(82.8%, 99.9%)	23	87.0% (20/23)	(66.4%, 97.2%)	22	86.4% (19/22)	(65.1%, 97.1%)
		GMC µg/mL	30	3.5	(2.1, 6.0)	23	2.8	(1.6, 4.9)	22	2.2	(1.1, 4.6)
7F	Predose	%>=level†	30	0.0% (0/30)	(0.0%, 11.6%)	24	4.2% (1/24)	(0.1%, 21.1%)	24	8.3% (2/24)	(1.0%, 27.0%)
		GMC µg/mL	30	0.0	(0.0, 0.1)	24	0.1	(0.0, 0.1)	24	0.1	(0.0, 0.2)
	Postdose	%>=level†	30	90.0% (27/30)	(73.5%, 97.9%)	23	100.0% (23/23)	(85.2%, 100.0%)	22	9.1% (2/22)	(1.1%, 29.2%)
		GMC µg/mL	30	2.0	(1.4, 3.0)	23	3.2	(2.2, 4.6)	22	0.1	(0.1, 0.2)
19A	Predose	%>=level†	30	16.7% (5/30)	(5.6%, 34.7%)	24	25.0% (6/24)	(9.8%, 46.7%)	24	29.2% (7/24)	(12.6%, 51.1%)
		GMC µg/mL	30	0.3	(0.2, 0.5)	24	0.4	(0.2, 0.6)	24	0.4	(0.3, 0.7)
	Postdose	%>=level†	30	83.3% (25/30)	(65.3%, 94.4%)	23	95.7% (22/23)	(78.1%, 99.9%)	22	72.7% (16/22)	(49.8%, 89.3%)
		GMC µg/mL	30	1.6	(1.1, 2.4)	23	2.3	(1.6, 3.4)	22	1.7	(1.0, 2.7)

Summary of IgG Antibody Responses to the Serotypes not in Common with Prevnar by Treatment Group Per Protocol Population Toddler Cohort

Pneumococcal Serotype	Time Point	Endpoint	V114 Aluminum Adjuvanted			V114 Nonadjuvanted			Prevnar		
			n	Observed response	95% CI	n	Observed response	95% CI	n	Observed response	95% CI
33F	Predose	%>=level†	30	0.0% (0/30)	(0.0%, 11.6%)	24	4.2% (1/24)	(0.1%, 21.1%)	24	0.0% (0/24)	(0.0%, 14.2%)
		GMC µg/mL	30	0.1	(0.0, 0.1)	24	0.1	(0.1, 0.1)	24	0.1	(0.0, 0.1)
	Postdose	%>=level†	30	63.3% (19/30)	(43.9%, 80.1%)	23	69.6% (16/23)	(47.1%, 86.8%)	22	0.0% (0/22)	(0.0%, 15.4%)
		GMC µg/mL	30	0.9	(0.6, 1.5)	23	1.1	(0.6, 1.9)	22	0.1	(0.1, 0.2)

†Serotype-specific IgG antibody concentration measured by the ECL assay corresponding to a level of 0.35 µg/mL in the WHO ELISA. This concentration is 0.59 µg/mL for all serotypes.
n = Number of subjects contributing to the analysis.
GMC = Geometric mean concentration.
CI = Confidence interval.

Safety:

Among adults, the safety profile of a single dose of aluminum-adjuvanted V114 was comparable to that of Prevnar™. Although subjects receiving V114 reported a numerically higher incidence of injection site and systemic adverse experiences than subjects who received Prevnar™, these differences were not statistically significant. They were also considered not clinically significant, as the adverse experiences were mostly transient and mild to moderate in intensity. Among toddlers, the safety profile of a booster dose of either aluminum-adjuvanted V114 or nonadjuvanted V114 was comparable to that of Prevnar™. Although subjects receiving either formulation of V114 reported a numerically higher incidence of injection site and systemic adverse experiences in comparison to subjects who received Prevnar™, these differences were not statistically significant. They were also considered not clinically significant, as the majority of the reported adverse experiences were mostly transient and of mild to moderate intensity. In addition, subjects receiving the aluminum-adjuvanted V114 reported a slightly numerically higher incidence of injection site and systemic adverse experiences than subjects who received nonadjuvanted V114.

Adverse Event Summary Day 1 to Day 14 Postvaccination Adult Cohort

	V114 adjuvanted		PREVNAR		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population with follow-up	30		30		60	
with one or more adverse events	28	(93.3)	25	(83.3)	53	(88.3)
injection-site	27	(90.0)	24	(80.0)	51	(85.0)
non-injection-site	24	(80.0)	18	(60.0)	42	(70.0)
with no adverse event	2	(6.7)	5	(16.7)	7	(11.7)
with vaccine-related† adverse events	28	(93.3)	25	(83.3)	53	(88.3)
injection-site	27	(90.0)	24	(80.0)	51	(85.0)
non-injection-site	21	(70.0)	14	(46.7)	35	(58.3)
with serious adverse events	0	(0.0)	0	(0.0)	0	(0.0)
with serious vaccine-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a vaccine-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious vaccine-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)

† Determined by the investigator to be related to the vaccine.
‡ Study medication withdrawn.
The term non injection-site adverse event corresponds to systemic adverse event.

Adverse Event Summary Day 1 to Day 14 Postvaccination Toddler Cohort

	V114 adjuvanted		V114 nonadjuvanted		PREVNAR		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population with follow-up	33		28		28		89	
with one or more adverse events	31	(93.9)	25	(89.3)	24	(85.7)	80	(89.9)
injection-site	24	(72.7)	18	(64.3)	16	(57.1)	58	(65.2)
non-injection-site	31	(93.9)	24	(85.7)	23	(82.1)	78	(87.6)
with no adverse event	2	(6.1)	3	(10.7)	4	(14.3)	9	(10.1)
with vaccine-related† adverse events	28	(84.8)	22	(78.6)	21	(75.0)	71	(79.8)
injection-site	24	(72.7)	18	(64.3)	16	(57.1)	58	(65.2)
non-injection-site	24	(72.7)	19	(67.9)	18	(64.3)	61	(68.5)
with serious adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with serious vaccine-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a vaccine-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious vaccine-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

† Determined by the investigator to be related to the vaccine.
‡ Study medication withdrawn.
The term non injection-site adverse event corresponds to systemic adverse event.

CONCLUSIONS: V114 adjuvanted and nonadjuvanted formulations display comparable safety and immunogenicity (for the shared serotypes) profiles to Prevnar™.

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