Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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1. Study inclusion and exclusion criteria

a. For study A conducted in healthy 12- to 23-month-olds

Inclusion Criteria
A subject will be eligible for inclusion if ALL of the following apply at the time of enrollment:

1. Age 12 to 23 months of age (both included);
2. Written informed consent obtained from the mother, father, or guardian of the child;
3. Free of obvious health problems as established by medical history including physical examination and clinical judgment of the investigator;
4. Mother, father, or guardian capable and willing to bring their child or to receive home visits for their child for all follow-up visits
5. Residence in the study area; and
6. Fully vaccinated according to local EPI schedule.

Exclusion Criteria
Subjects with any of the following criteria at study entry will not be eligible for participation:

1. Previous vaccination against serogroup A *Neisseria meningitidis*;
2. Known exposure to serogroup A *Neisseria meningitidis* during the three previous months;
3. History of allergic disease or known hypersensitivity to any component of the three study vaccines;
4. History of Serious Adverse Reactions following administration of vaccines included in the local program of immunization;
5. Administration of any other vaccine within 60 days prior to administration of study vaccines or planned vaccination during the first four weeks after the study vaccination;
6. Use of any investigational or nonregistered drug within 90 days prior to the administration of study vaccines;
7. Administration of immunoglobulins and/or any blood products since birth or planned administration during the vaccine period;
8. Chronic administration (defined as more than 14 days) of immunosuppressants or other immune-modifying agents since birth (Including systemic or inhaled corticosteroids, this means prednisone, or equivalent, ≥ 0.5 mg/kg/day; topical steroids are allowed);

9. A family history of congenital or hereditary immunodeficiency;
10. History of meningitis or seizures or any neurological disorder;
11. Major congenital defects or serious chronic illness, including malnutrition (as per investigator's judgment);
12. Acute disease at the time of enrollment (acute disease is defined as the presence of a moderate or severe illness with or without fever) is a **temporary exclusion**;
13. Acute or chronic, clinically significant pulmonary, cardiovascular, hepatic, or renal functional abnormality, as determined by medical history, physical examination or laboratory tests, which in the opinion of the investigator, might interfere with the study objectives;
14. Any condition or criteria that in the opinion of the investigator might compromise the well being of the subject or the compliance with study procedures or interfere with the outcome of the study; or
15. Nonresidence in the study area or intent to move out within 1 year.

b. For study B conducted in healthy 2- to 29-year-olds

Inclusion Criteria

A subject will be eligible for inclusion if ALL of the following apply at the time of enrollment:

1. Age 2 to 29 years of age (both included);
2. Written informed consent obtained from the subject (for subjects ≥18 years of age) / parents or legal guardian (for subjects <18 years of age);
3. Written informed assent from the subject if and as appropriate within the participating community (e.g. for subjects ≥ 13 years of age in the Malian site, for subjects ≥ 15 years of age in the Senegal site or for subject ≥ 12 years of age in the Gambia site);
4. Free of obvious health problems as established by medical history including physical examination and clinical judgment of the investigator;
5. Subject / parents, or legal guardian capable and willing to come / bring their child or to receive home visits for all follow-up visits;
6. Residence in the study area; and
7. Fully vaccinated according to the local EPI schedule (for subjects 2 to 3 years of age only).

Exclusion Criteria

Subjects with any of the following criteria at study entry will not be eligible for participation:

1. Previous vaccination against *Neisseria meningitidis* during the six previous years;
2. Known exposure to *Neisseria meningitidis* during the three previous months;

3. History of allergic disease or known hypersensitivity to any component of the two study vaccines and/or following administration of vaccines included in the local program of immunization;
4. Administration of any other vaccine within 60 days prior to administration of study vaccines or planned vaccination during the first 28 days after the study vaccination;
5. Use of any investigational or nonregistered drug within 90 days prior to the administration of study vaccines;
6. Administration of immunoglobulins and/or any blood products within 30 days prior to the administration of study vaccines or planned administration during the study period;
7. Chronic administration (defined as more than 14 days) of immunosuppressants or other immune-modifying agents within 90 days prior to the administration of study vaccines (Including systemic corticosteroids, this means prednisone, or equivalent, ≥ 0.5 mg/kg/day; topical steroids including inhaled steroids are allowed);
8. A family history of congenital or hereditary immunodeficiency;
9. History of meningitis or seizures or any neurological disorder;
10. Major congenital defects or serious chronic illness, including malnutrition (as per investigator's judgment);
11. Acute disease at the time of enrollment (acute disease is defined as the presence of a moderate or severe illness with or without fever) is a **temporary exclusion**;
12. Acute or chronic, clinically significant pulmonary, cardiovascular, hepatic, or renal functional abnormality, as determined by medical history, physical examination or laboratory tests, which in the opinion of the investigator, might interfere with the study objectives;
13. Any condition or criteria that in the opinion of the investigator might compromise the well being of the subject or the compliance with study procedures or interfere with the outcome of the study;
14. Nonresidence in the study area or intent to move out within 1 year;
15. Pregnancy or lactation (a negative pregnancy test will be required before vaccination for all women of childbearing potential); or
16. Previous inclusion of five family members in the study (i.e. subjects belonging to the same family - biological father, mother, child, and brothers and sisters may be included up to a maximum of five members from the same family).

2. Ethical and Regulatory Clearances

Ethical approval was granted by The Gambia joint Government/MRC Ethics Committee, the Senegal Ministry of Health “Conseil National de la Recherche en Santé” and the IRD “Comité consultatif de déontologie et d’éthique” (Paris, France), and the Mali University of Bamako “Faculté de Médecine de Pharmacie et d’Odonto-Stomatologie” Ethics Committee and the University of Maryland School of Medicine Human Research Protections Office (Baltimore, USA). The Research Ethics Committees at WHO (ERC) and PATH (REC for study A or Western Institutional Review Board, Olympia, WA, USA for study B) also approved the study documents. National regulatory authorities of each country also gave study approval.

3. Data Safety Monitoring Boards

An independent three person Data Safety Monitoring Board (DSMB) was established prior to initiating each study with the purpose of reviewing all available information on safety and advising the sponsor on any concerns related to vaccine safety. The DSMB thoroughly assessed safety throughout each study period to ensure the protection of human subjects, operating according to each study DSMB charter, i.e. in accordance with ICH and WHO guidelines as well as regulatory guidelines (Indian DCGI, EMEA, and FDA) for the operation of such boards. The composition of the DSMB was the same for both studies: Dr. Jean-François Etard (voting member 1, chair), Prof. Andrew J Hall (voting member 2) and Mrs. Aissata Doumbia Diarra (voting member 3).

4. Study sample size calculations

a. For study A conducted in healthy 12-to 23-month-olds

Sample Size

Sample size calculations for the comparison of proportions using a noninferiority model are detailed in this section. With this model, the null hypothesis is that Group 1 (PsA-TT conjugate vaccine – the study vaccine [SV]) will have a significantly lower proportion of 4-fold response in postimmunization serum titer with respect to preimmunization serum titer than in Group 2 (ACWY polysaccharide vaccine – the reference vaccine [RV]). The alternative hypothesis is that Group 1 is noninferior to Group 2. If the null hypothesis is rejected then we may conclude, with stated power and level of significance, that Group 1 is noninferior to Group 2 in terms of proportion of 4-fold response in MenPsA rSBA antibody titers.

The following calculations detail the necessary number of subjects needed within each group to have the specified power to reject the null hypothesis of inferiority. In this study, we propose a 95% one sided, noninferiority hypothesis which is that p (reference vaccine) - p (study vaccine) ≥ 0.10:

The null hypothesis, H_0: p(RV) - p(SV) >= 0.10 (Inferior)
The alternative hypothesis, H_1: p(RV) - p(SV) < 0.10 (Noninferior)

where RV = the ACWY polysaccharide vaccine Group 2 and SV = the PsA-TT conjugate vaccine Group 1.

Reject H_0 when the upper 95.0% confidence bound for the difference (p (RV) - p (SV)) is < 0.10.

Sample size calculations were based on formulas derived from Farrington and Manning. The method of maximum likelihood (Method 3) was used to compute the variance of the difference under the null hypothesis. Farrington and Manning recommend this method for calculating the most accurate sample sizes.

The sample size specified assuming p(RV) = 0.90 under the null hypothesis and with a 95% one-sided hypothesis and 80% power is 155 in each study group. Inflating this number to account for a 22.5% drop-out rate leads to a final sample size of 200 for each study group.

b. For study B conducted in healthy 2- to 29-year-olds

Sample Size

Sample size calculations for the comparison of proportions using a noninferiority model are detailed in this section. With this model, the null hypothesis is that Group 1 (PsA-TT conjugate vaccine – the Study vaccine [SV]) will have a significantly lower proportion of 4-fold response in postimmunization serum titer with respect to preimmunization serum titer than Group 2 (ACWY polysaccharide vaccine – the reference vaccine [RV]). The alternative hypothesis is that Group 1 is noninferior to Group 2. If the null hypothesis is rejected then it may be concluded, with stated power and level of significance, that Group 1 is noninferior to Group 2 in terms of proportion of 4-fold response in MenPsA rSBA antibody titers.
The following calculations detail the necessary number of subjects needed within each group to have the specified power to reject the null hypothesis of inferiority:

The null hypothesis, H_0: $p(RV) - p(SV) \geq 0.10$ (Inferior)
The alternative hypothesis, H_1: $p(RV) - p(SV) < 0.10$ (Noninferior)

where RV = the ACWY polysaccharide vaccine Group 2 and SV = the PsA-TT conjugate vaccine Group 1.

Reject H_0 when the upper bound of the 95% confidence interval about the difference (p (RV) - p (SV)) is < 0.10.

Sample size calculations were based on formulas derived from Farrington and Manning. Farrington and Manning recommend this method for calculating the most accurate sample sizes. The sample size is calculated under following assumptions:
o p(RV) = 0.90 under the null hypothesis
o Power = 80%
o One sided $\alpha = 0.025$
o Subject distribution ratio between Study Vaccine (SV) to Reference Vaccine (RV) is 2:1

Under these assumptions, 193 evaluable subjects for SV group and 97 evaluable subjects for RV group are required, thus a total 290 evaluable subjects. Since three groups are further considered as per age stratification with equal distribution of subjects, to facilitate further comparison this sample size is extrapolated to 870 (290x3 = 870). The total sample size becomes 900 taking into account a drop-out rate of approximately 3% i.e. negligible because no drop-outs are expected since the primary end point is being assessed immediately at day 28 to check noninferiority of the study vaccine.

5. Demographics and clinical characteristics of the study subjects for study A and study B (Supplementary Appendix Table 1.)

Supplementary Appendix Table 1a. Demographics and clinical characteristics for study A conducted in healthy 12- to 23-month-olds

Immunization	Vaccine group	N	Median age, months (mix-max)	female n (%)	Median height, cm (min-max)	Median weight, kg (min-max)	Malaria thick smear test positive n (%)
Primary	PsA-TT	201	17 (11*-23)	92 (45.8)	78 (68-90)	9.2 (6.0-14.0)	9 (4.5)
	PsACWY	200	18 (12-23)	91 (45.5)	79 (70-92)	9.3 (6.4-14.2)	11 (5.5)
	Hib-TT	200	18 (12-23)	96 (48)	79 (67-105)	9.3 (6.0-14.0)	13 (6.5)
Booster	PsA-TT/PsA-TT	64	26 (20-33)	34 (53.1)	85 (76-97)	10.6 (8.0-14.0)	1 (1.6)
	PsA-TT/PsACWY	67	26 (20-32)	29 (43.3)	85 (73-96)	11.0 (8.0-14.0)	2 (3.0)
	PsA-TT/Hib-TT	66	25 (21-32)	29 (43.9)	84 (74-96)	10.6 (7.4-15.0)	0 (0.0)
	PsACWY/PsA-TT	65	27 (21-32)	31 (47.7)	85 (75-93)	10.6 (8.0-14.0)	1 (1.6)
	PsACWY/PsACWY	64	27 (21-32)	26 (40.6)	86 (76-96)	11.0 (8.0-17.0)	1 (1.6)
	PsACWY/Hib-TT	68	25 (20-32)	32 (47.1)	85 (79-93)	11.0 (9.0-16.2)	0 (0.0)
	Hib-TT /PsA-TT	63	26 (20-33)	27 (42.9)	85 (77-97)	10.8 (8.3-14.5)	2 (3.2)
	Hib-TT /PsACWY	66	26 (20-32)	33 (50)	85 (79-97)	11.0 (8.0-14.0)	0 (0.0)
	Hib-TT /Hib-TT	66	28 (20-32)	35 (53.0)	86 (76-98)	11.0 (8.0-15.0)	0 (0.0)

* One subject was vaccinated 1 day before his 12-month birthday due to an initial typographical error in his date of birth.

Supplementary Appendix Table 1b. Demographics and clinical characteristics for study B conducted in healthy 2- to 29-year-olds

Age group	Vaccine group	N	Median age, years (min-max)	female n (%)	Median height, cm (min-max)	Median weight, kg (min-max)	Malaria thick smear test positive n (%)
2-10 yrs	PsA-TT	203	7 (2-10)	101 (49.8)	119 (76-159)	19.0 (9.0-48.0)	9 (4.4)
	PsACWY	99	6 (2-10)	47 (47.5)	116 (80-155)	17.0 (10.0-41.0)	6 (6.1)
11-17 yrs	PsA-TT	202*	14 (11-17)	75 (37.1)	153 (129-183)	39.0 (20.4-69.0)	10 (5.0)
	PsACWY	99	14 (11-17)	39 (39.4)	150 (126-182)	37.0 (19.0-64.0)	14 (14.1)
18-29 yrs	PsA-TT	199	20 (18-29)	74 (37.2)	170 (144-192)	56.0 (37.0-88.0)	7 (3.5)
	PsACWY	98	20 (18-29)	36 (36.7)	172 (151-190)	60.0 (37.4-82.0)	5 (5.1)
Total	PsA-TT	604*	14 (2-29)	250 (41.4)	152 (76-192)	39.0 (9.0-88.0)	26 (4.3)†
	PsACWY	296	14 (2-29)	122 (41.2)	151 (80-190)	37.0 (10.0-82.0)	25 (8.4)†

* There was one missing value for weight.

† P = 0.0115 for the comparison of PsACWY vs. PsA-TT using CMH test adjusting for age group.

6. Supplementary Immunogenicity Tables

a. Supplementary Appendix Table 2. Proportion of subjects with meningococcal group A 4-fold rSBA response and 4-fold IgG (ELISA) response with reference to baseline (preimmunization) for study A and study B

Supplementary Appendix Table 2a. Proportion of subjects with 4-fold rSBA response and 4-fold IgG (ELISA) response for study A conducted in healthy 12-to 23-month-olds

Vaccine group		Week 4 (28 days postprimary)			Week 40 * (prebooster)			Week 41 (7 days postbooster)			Week 44 (28 days postbooster)		
Primary	Booster	n/N	%	(95% CI)	n/N	%	(95% CI)	n/N	%	(95% CI)	n/N	%	(95% CI)
					4-fold rSBA response								
PsA-TT	PsA-TT	190/198	96.0	(92.2-98.2)	53/63	84.1	(72.7-92.1)	59/59	100	(93.9-100.0)	57/58	98.3	(90.8-100.0)
	PsACWY				57/67	85.1	(74.3-92.6)	57/60	95	(86.1-99.0)	61/63	96.8	(89.0-99.6)
	Hib-TT				50/65	76.9	(64.8-86.5)	52/64	81.3	(69.5-89.9)	57/64	89.1	(78.8-95.5)
PsACWY	PsA-TT	123/193	63.7	(56.5-70.5)	25/64	39.1	(27.1-52.1)	57/59	96.6	(88.3-99.6)	57/59	96.6	(88.3-99.6)
	PsACWY				26/64	40.6	(28.5-53.6)	51/61	83.6	(71.9-91.8)	43/62	69.4	(56.3-80.4)
	Hib-TT				24/68	35.3	(24.1-47.8)	32/65	49.2	(36.6-61.9)	35/66	53.0	(40.3-65.4)
Hib-TT	PsA-TT	69/194	35.6	(28.8-42.7)	24/62	38.7	(26.6-51.9)	58/58	100	(93.8-100.0)	56/57	98.2	(90.6-100.0)
	PsACWY				27/66	40.9	(29.0-53.7)	60/64	93.8	(84.8-98.3)	55/64	85.9	(75.0-93.4)
	Hib-TT				23/65	35.4	(23.9-48.2)	24/59	40.7	(28.1-54.3)	36/60	60	(46.5-72.4)
					4-fold group A-specific IgG response								
PsA-TT	PsA-TT	197/198	99.5	(97.2-100.0)	51/63	81.0	(69.1-89.8)	58/59	98.3	(90.9-100.0)	55/58	94.8	(85.6-98.9)
	PsACWY				52/67	77.6	(65.8-86.9)	59/60	98.3	(91.1-100.0)	62/63	98.4	(91.5-100.0)
	Hib-TT				46/64	71.9	(59.2-82.4)	46/63	73.0	(60.3-83.4)	45/63	71.4	(58.7-82.1)
PsACWY	PsA-TT	152/194	78.4	(71.9-83.9)	30/63	47.6	(34.9-60.6)	58/58	100	(93.8-100.0)	58/58	100	(93.8-100.0)
	PsACWY				31/64	48.4	(35.8-61.3)	53/61	86.9	(75.8-94.2)	53/62	85.5	(74.2-93.1)
	Hib-TT				30/68	44.1	(32.1-56.7)	35/65	53.8	(41.0-66.3)	31/66	47.0	(34.6-59.7)
Hib-TT	PsA-TT	7/194	3.6	(1.5-7.3)	4/63	6.3	(1.8-15.5)	57/59	96.6	(88.3-99.6)	57/58	98.3	(90.8-100.0)
	PsACWY				3/64	4.7	(1.0-13.1)	55/63	87.3	(76.5-94.4)	52/63	82.5	(70.9-90.9)
	Hib-TT				10/65	15.4	(7.6-26.5)	6/59	10.2	(3.8-20.8)	6/60	10	(3.8-20.5)

* The proportions of 4-fold rSBA responders at week 40 were 82.1% (95% CI 75.9-87.2) for PsA-TT, 38.3% (95% CI 31.4-45.5) for PsACWY, and 38.3% (95% CI 31.5-45.6) for Hib-TT;

The proportions of 4-fold IgG responders at week 40 were 76.8% (95% CI 70.2-82.5) for PsA-TT, 46.7% (95% CI 39.5-53.9) for PsACWY, and 8.9% (95% CI 5.2-13.8) for Hib-TT.

Note: The difference in proportions of 4-fold rSBA responders between PsACWY and PsA-TT at week 4 (study primary endpoint for noninferiority) and week 40 was -32% (95% CI -40 - -25) and -44% (95% CI -52 - -35), respectively;

The difference in proportions of 4-fold IgG responders between PsACWY and PsA-TT at week 4 and week 40 was -21% (95% CI -28 - -16) and -30% (95% CI -39 - -21), respectively.

Supplementary Appendix Table 2b. Proportion of subjects with 4-fold rSBA response and 4-fold IgG (ELISA) response for study B conducted in healthy 2- to 29-year-olds

Age group	Vaccine group	Week 4 (28 days postimmunization)		
		n/N	%	(95% CI)
	4-fold rSBA response			
2-10 yrs	PsA-TT	172/202	85.1	(79.5-89.8)
	PsACWY	52/97	53.6	(43.2-63.8)
11-17 yrs	PsA-TT	155/202	76.7	(70.3-82.4)
	PsACWY	39/99	39.4	(29.7-49.7)
18-29 yrs	PsA-TT	144/198	72.7	(66.0-78.8)
	PsACWY	43/94	45.7	(35.4-56.3)
Total	PsA-TT	471/602	78.2	(74.7-81.5)
	PsACWY	134/290	46.2	(40.4-52.1)
	4-fold group A-specific IgG response			
2-10 yrs	PsA-TT	195/199	98.0	(94.9-99.4)
	PsACWY	84/96	87.5	(79.2-93.4)
11-17 yrs	PsA-TT	187/202	92.6	(88.0-95.8)
	PsACWY	55/99	55.6	(45.2-65.5)
18-29 yrs	PsA-TT	149/198	75.3	(68.6-81.1)
	PsACWY	33/94	35.1	(25.5-45.6)
Total	PsA-TT	531/599	88.6	(85.8-91.1)
	PsACWY	172/289	59.5	(53.6-65.2)

Note: The difference in proportions of 4-fold rSBA responders between PsACWY and PsA-TT at week 4 (study primary endpoint for noninferiority) was -32% (95% CI -39 - -25);

The difference in proportions of 4-fold IgG responders between PsACWY and PsA-TT at week 4 was -29% (95% CI -35 - 23).

b. *Supplementary Appendix Table 3. Meningococcal group A rSBA geometric mean titers and IgG geometric mean concentrations with 95% confidence intervals per age group for study B*

Supplementary Appendix Table 3. rSBA GMTs and Group A-specific IgG GMCs for study B conducted in healthy 2- to 29-year-olds

Age group	Vaccine group	Week 0 (preimmunization)		Week 4 (28 days postimmunization)	
		rSBA GMTs (95% CI)			
2-10 yrs	PsA-TT	209.8	(144.4-304.7)	6743.2	(5900.7-7705.9)
	PsACWY	233.3	(140.3-388.0)	1290.2	(882.4-1886.4)
11-17 yrs	PsA-TT	264.9	(187.7-374.0)	4618.7	(4029.4-5294.2)
	PsACWY	426.8	(267.7-680.4)	1137.4	(803.6-1609.8)
18-29 yrs	PsA-TT	199.9	(138.5-288.6)	3331.6	(2872.3-3864.4)
	PsACWY	314.9	(200.3-495.3)	1150.8	(805.7-1643.8)
Total	PsA-TT	223.3	(181.3-274.9)	4712.6	(4336.0-5122.0)
	PsACWY	316.0	(240.4-415.3)	1191.4	(969.1-1464.6)
		Group A-specific IgG GMCs (95% CI) (µg/mL)			
2-10 yrs	PsA-TT	0.5	(0.4-0.6)	57.7	(49.7-67.1)
	PsACWY	0.4	(0.3-0.5)	7.2	(5.5-9.4)
11-17 yrs	PsA-TT	3.7	(3.1-4.5)	78.4	(67.5-91.1)
	PsACWY	2.8	(2.1-3.8)	15.5	(11.5-21.0)
18-29 yrs	PsA-TT	5.6	(4.7-6.7)	62.1	(53.1-72.7)
	PsACWY	6.1	(4.6-8.1)	19.6	(14.8-25.9)
Total	PsA-TT	2.1	(1.9-2.5)	65.6	(60.0-71.6)
	PsACWY	1.9	(1.5-2.3)	12.9	(10.9-15.3)

Note: $P < 0.0001$ for the comparisons of PsACWY vs. PsA-TT in rSBA GMT and IgG GMC at week 4 using t-test.

c. Supplementary Appendix Table 4. Proportion of subjects with meningococcal group A rSBA titer ≥ 1:128 and IgG (ELISA) concentration ≥ 2 µg/ml for study A and study B

Supplementary Appendix Table 4a. Proportion of subjects with rSBA titer ≥ 1:128 and IgG (ELISA) concentration ≥ 2µg/mL for study A conducted in healthy 12- to 23-month-olds

Vaccine group		Week 0 (preprimary)			Week 4 (28 days postprimary)			Week 40 * (prebooster)			Week 41 (7 days postbooster)			Week 44 (28 days postbooster)		
Primary	**Booster**	**n/N**	**%**	**(95% CI)**	**n/N**	**%**	**(95% CI)**	**n/N**	**%**	**(95% CI)**	**n/N**	**%**	**(95% CI)**	**n/N**	**%**	**(95% CI)**
								rSBA titer ≥ 1:128								
PsA-TT	PsA-TT	70/201	34.8	(28.3-41.8)	193/198	97.5	(94.2-99.2)	58/63	92.1	(82.4-97.4)	59/59	100	(93.9-100.0)	58/58	100	(93.8-100.0)
	PsACWY							64/67	95.5	(87.5-99.1)	60/60	100	(94.0-100.0)	63/63	100	(94.3-100.0)
	Hib-TT							58/65	89.2	(79.1-95.6)	61/64	95.3	(86.9-99.0)	61/64	95.3	(86.9-99.0)
PsACWY	PsA-TT	68/200	34	(27.5-41.0)	154/193	79.8	(73.4-85.2)	35/64	54.7	(41.7-67.2)	59/59	100	(93.9-100.0)	59/59	100	(93.9-100.0)
	PsACWY							36/64	56.3	(43.3-68.6)	61/61	100	(94.1-100.0)	55/62	88.7	(78.1-95.3)
	Hib-TT							36/68	52.9	(40.4-65.2)	44/65	67.7	(54.9-78.8)	47/66	71.2	(58.7-81.7)
Hib-TT	PsA-TT	61/199	30.7	(24.3-37.6)	112/195	57.4	(50.2-64.5)	33/63	52.4	(39.4-65.1)	59/59	100	(93.9-100)	58/58	100	(93.8-100.0)
	PsACWY							38/66	57.6	(44.8-69.7)	64/64	100	(94.4-100.0)	61/64	95.3	(86.9-99.0)
	Hib-TT							34/65	52.3	(39.5-64.9)	36/59	61.0	(47.4-73.5)	46/60	76.7	(64.0-86.6)
								group A-specific IgG concentration ≥ 2 µg/mL								
PsA-TT	PsA-TT	3/200	1.5	(0.3-4.3)	198/199	99.5	(97.2-100.0)	16/63	25.4	(15.3-37.9)	58/59	98.3	(90.9-100.0)	55/58	94.8	(85.6-98.9)
	PsACWY							22/67	32.8	(21.8-45.4)	59/60	98.3	(91.1-100.0)	62/63	98.4	(91.5-100.0)
	Hib-TT							24/65	36.9	(25.3-49.8)	25/64	39.1	(27.1-52.1)	23/64	35.9	(24.3-48.9)
PsACWY	PsA-TT	0/199	0	(0.0-1.8)	85/195	43.6	(36.5-50.9)	8/64	12.5	(5.6-23.2)	59/59	100	(93.9-100.0)	59/59	100	(93.9-100.0)
	PsACWY							14/64	21.9	(12.5-34.0)	38/61	62.3	(49.0-74.4)	39/62	62.9	(49.7-74.8)
	Hib-TT							12/68	17.6	(9.5-28.8)	12/65	18.5	(9.9-30.0)	9/66	13.6	(6.4-24.3)
Hib-TT	PsA-TT	2/198	1	(0.1-3.6)	3/196	1.5	(0.3-4.4)	0/63	0	(0.0-5.7)	56/59	94.9	(85.9-98.9)	56/58	96.6	(88.1-99.6)
	PsACWY							3/65	4.6	(1.0-12.9)	30/64	46.9	(34.3-59.8)	28/64	43.8	(31.4-56.7)
	Hib-TT							2/65	3.1	(0.4-10.7)	2/59	3.4	(0.4-11.7)	2/60	3.3	(0.4-11.5)

* The proportions of subjects with rSBA titer ≥ 1:128 at week 40 were 92.3% (95% CI 87.6-95.6) for PsA-TT, 54.6% (95% CI 47.3-61.7) for PsACWY, and 54.1% (95% CI 46.8-61.3) for Hib-TT;

The proportions of subjects with IgG concentration ≥ 2µg/mL at week 40 were 31.8% (95% CI 25.3-38.8) for PsA-TT, 17.3% (95% CI 12.3-23.4) for PsACWY, and 2.6% (95% CI 0.8-5.9) for Hib-TT.

Note: P < 0.0001 for the comparisons of PsACWY vs. PsA-TT groups in cutoffs of 1:128 and 2µg/ml at week 4 and week 40 using Fisher's exact test. The similar trend was observed for the rSBA titer cutoff of 1:8.

Supplementary Appendix Table 4b. Proportion of subjects with rSBA titer ≥ 1:128 and IgG (ELISA) concentration ≥ 2µg/mL for study B conducted in healthy 2- to 29-year-olds

Age group	Vaccine group	Week 0 (preimmunization)			Week 4 (28 days postimmunization)		
		n/N	%	(95% CI)	n/N	%	(95% CI)
				rSBA titer ≥ 1:128			
2-10 yrs	PsA-TT	155/202	76.7	(70.3-82.4)	203/203	100	(98.2-100.0)
	PsACWY	77/97	79.4	(70.0-86.9)	93/99	93.9	(87.3-97.7)
11-17 yrs	PsA-TT	155/202	76.7	(70.3-82.4)	202/202	100	(98.2-100.0)
	PsACWY	85/99	85.9	(77.4-92.0)	93/99	93.9	(87.3-97.7)
18-29 yrs	PsA-TT	150/199	75.4	(68.8-81.2)	197/198	99.5	(97.2-100.0)
	PsACWY	81/97	83.5	(74.6-90.3)	89/95	93.7	(86.8-97.6)
Total	PsA-TT	460/603	76.3	(72.7-79.6)	602/603	99.8	(99.1-100.0)
	PsACWY	243/293	82.9	(78.1-87.1)	275/293	93.9	(90.5-96.3)
				group A-specific IgG concentration ≥ 2 µg/mL			
2-10 yrs	PsA-TT	39/202	19.3	(14.1-25.4)	200/200	100	(98.2-100.0)
	PsACWY	16/97	16.5	(9.7-25.4)	77/98	78.6	(69.1-86.2)
11-17 yrs	PsA-TT	136/202	67.3	(60.4-73.7)	202/202	100	(98.2-100.0)
	PsACWY	56/99	56.6	(46.2-66.5)	89/99	89.9	(82.2-95.0)
18-29 yrs	PsA-TT	151/199	75.9	(69.3-81.6)	198/198	100	(98.2-100.0)
	PsACWY	77/97	79.4	(70.0-86.9)	91/95	95.8	(89.6-98.8)
Total	PsA-TT	326/603	54.1	(50.0-58.1)	600/600	100	(99.4-100.0)
	PsACWY	149/293	50.9	(45.0-56.7)	257/292	88.0	(83.7-91.5)

Note: P < 0.0001 for the comparisons of PsACWY vs. PsA-TT in the cutoffs of 1:128 and 2µg/mL at week 4 using CMH test adjusting for age group. The similar trend was observed for the rSBA titer cutoff of 1:8.

7. Supplementary Safety Tables

a. Supplementary Appendix Table 5. Overall participant safety profile postimmunisation per age group for study B

Supplementary Appendix Table 5. Safety profile postimmunization for study B conducted in healthy 2- to 29-year-olds

Age group	Vaccine group		Local Reaction within 4 days post-immunization			Systemic Reaction† within 4 days post-immunization			Adverse Event within 28 days post-immunization			Serious Adverse Event within 392 days post-immunization		
		N	n	%	(95% CI)	n	%	(95% CI)	n	%	(95% CI)	n	%	(95% CI)
2-10 yrs	PsA-TT	203	11	5.4	(2.7-9.5)	7	3.4	(1.4-7.0)	17	8.4	(5.0-13.1)	0	0	(0.0-1.8)
	PsACWY	99	2	2.0	(0.2-7.1)	2	2.0	(0.2-7.1)	11	11.1	(5.7-19.0)	1	1.0	(0.0-5.5)
11-17 yrs	PsA-TT	202	11	5.4	(2.7-9.5)	6	3.0	(1.1-6.4)	21	10.4	(6.6-15.5)	0	0	(0.0-1.8)
	PsACWY	99	2	2.0	(0.2-7.1)	1	1.0	(0.0-5.5)	12	12.1	(6.4-20.2)	0	0	(0.0-3.7)
18-29 yrs	PsA-TT	199	12	6.0	(3.2-10.3)	5	2.5	(0.8-5.8)	18	9.0	(5.4-13.9)	2	1.0	(0.1-3.6)
	PsACWY	98	1	1.0	(0.0-5.6)	2	2.0	(0.2-7.2)	5	5.1	(1.7-11.5)	2	2.0	(0.2-7.2)
Total	PsA-TT	604	34	5.6*	(3.9-7.8)	18	3.0	(1.8-4.7)	56	9.3	(7.1-11.9)	2	0.3	(0.0-1.2)
	PsACWY	296	5	1.7*	(0.6-3.9)	5	1.7	(0.6-3.9)	28	9.5	(6.4-13.4)	3	1.0	(0.2-2.9)

* P = 0.0065 for the comparison of PsACWY vs. PsA-TT using CMH test adjusting for age group. The difference was due to more tenderness reported in PsA-TT than PsACWY group.

† Systemic reaction reported in the table includes fever, vomiting and diarrhea. Among 2- to 10-years age group, 2.0% of subjects (n/N 4/203, 95% CI 0.5-5.0) in PsA-TT group and 3.0% of subjects (n/N 3/99, 95% CI 0.6-8.6) in PsACWY group reported at least one of lethargy, irritability, and loss of appetite within 4 days postimmunization. In 11- to 17-years age group 11.4% of subjects (n/N 23/202, 95% CI 7.4-16.6) in PsA-TT and 10.1% of subjects (n/N 10/99, 95% CI 5.0-17.8) in PsACWY and in 18- to 29-years age group 13.6% of subjects (n/N 27/199, 95% CI 9.1-19.1) in PsA-TT and 16.3% of subjects (n/N 16/98, 95% CI 9.6-25.2) in PsACWY reported at least one of headache, fatigue, myalgia, and arthralgia within 4 days postimmunization.

b. Supplementary Appendix Table 6. Proportion of subjects with local postimmunization reactions 4 days after vaccination for study A and study B

The severity of the reactogenicity identified was assessed using the following intensity grade parameters.
For Tenderness
0 None
1 Minor light reaction to touch / Mild pain to touch (no disruption of normal daily activities).
2 Cried or protested to touch / Significant pain to touch (interferes with normal daily activities).
3 Cried when injected limb was moved / Significant pain on moving the limb (prevents normal daily activities).

For Induration (diameter in mm was measured)
0 Not present (≤ 5mm)
1 > 5mm
2 ≥ 20mm
3 ≥ 50mm

Supplementary Appendix Table 6a. Proportion of subjects with local post-immunization reactions for study A conducted in healthy 12- to 23-month-olds

Immunization	Vaccine group	Tenderness					Induration			
		All Grades (1,2,3)				Grades 2 or 3	All Grades (0,1,2,3)			Grades 2 or 3
		N	n	%	(95% CI)	n	n	%	(95% CI)	n
Primary	PsA-TT	201	13	6.5	(3.5-10.8)	1	16*	8.0	(4.6-12.6)	2
	PsACWY	200	9	4.5	(2.1-8.4)	2	4*	2	(0.5-5.0)	0
	Hib-TT	200	12	6	(3.1-10.2)	0	11	5.5	(2.8-9.6)	2
Booster	PsA-TT/PsA-TT	64	2	3.1	(0.4-10.8)	0	1	1.6	(0.0-8.4)	0
	PsA-TT/PsACWY	67	0	0	(0.0-5.4)	0	0	0	(0.0-5.4)	0
	PsA-TT/Hib-TT	66	0	0	(0.0-5.4)	0	0	0	(0.0-5.4)	0
	PsACWY/PsA-TT	65	1	1.5	(0.0-8.3)	0	0	0	(0.0-5.5)	0
	PsACWY/PsACWY	64	0	0	(0.0-5.6)	0	0	0	(0.0-5.6)	0
	PsACWY/Hib-TT	68	1	1.5	(0.0-7.9)	0	1	1.5	(0.0-7.9)	0
	Hib-TT/PsA-TT	63	1	1.6	(0.0-8.5)	0	0	0	(0.0-5.7)	0
	Hib-TT/PsACWY	66	0	0	(0.0-5.4)	0	0	0	(0.0-5.4)	0
	Hib-TT/Hib-TT	66	1	1.5	(0.0-8.2)	0	0	0	(0.0-5.4)	0

* P = 0.0099 for the comparison of PsACWY vs. PsA-TT using Fisher's exact test.

For primary immunization, only 1 Grade 3 Induration was reported in Hib-TT group and no Grade 3 Tenderness was reported.

Supplementary Appendix Table 6b. Proportion of subjects with local post-immunization reactions for study B conducted in healthy 2- to 29-year-olds

Age group	Vaccine group	Tenderness					Induration			
		All Grades (1,2,3)				Grades 2 or 3	All Grades (0,1,2,3)			Grades 2 or 3
		N	n	%	(95% CI)	n	n	%	(95% CI)	n
2-10 yrs	PsA-TT	203	9	4.4	(2.0-8.2)	1	4	2.0	(0.5-5.0)	0
	PsACWY	99	1	1.0	(0.0-5.5)	0	1	1.0	(0.0-5.5)	0
11-17 yrs	PsA-TT	202	9	4.5	(2.1-8.3)	0	3	1.5	(0.3-4.3)	1
	PsACWY	99	2	2.0	(0.2-7.1)	0	0	0	(0.0-3.7)	0
18-29 yrs	PsA-TT	199	12	6.0	(3.2-10.3)	0	0	0	(0.0-1.8)	0
	PsACWY	98	1	1.0	(0.0-5.6)	0	0	0	(0.0-3.7)	0
Total	PsA-TT	604	30*	5.0	(3.4-7.0)	1	7	1.2	(0.5-2.4)	1
	PsACWY	296	4*	1.4	(0.4-3.4)	0	1	0.3	(0.0-1.9)	0

* P = 0.0076 for the comparison of PsACWY vs. PsA-TT using CMH test adjusting for age group.

No Grade 3 local reactions were reported for either Tenderness or Induration.

c. *Supplementary Appendix Table 7. Proportion of subjects with systemic postimmunization reactions 4 days after vaccination for study A and study B*

The severity of the reactogenicity identified was assessed using the following intensity grade parameters.
For Fever (axillary temperature of ≥38℃)
0 Not Present (<38℃)
1 ≥38℃ to ≤38.9℃
2 ≥39℃ to ≤39.9℃
3 ≥40℃

For Other systemic post-immunization reactions
0 Not Present
1 Discomfort noted, but no disruption of normal daily activities; slightly bothersome; relieved with or without symptomatic treatment.
2 Discomfort sufficient to reduce or affect normal daily activity to some degree; bothersome; interferes with activities, only partially relieved with symptomatic treatment.
3 Discomfort sufficient to reduce or affect normal daily activity considerably (prevents regular activities for at least 24 hours); not relieved with symptomatic treatment, would cause subject or parent/legal guardian to seek medical advice.

Supplementary Appendix Table 7a. Proportion of subjects with systemic postimmunization reactions for study A conducted in healthy 12- to 23-month-olds

Immunization	Vaccine group		Fever				Vomiting			Diarrhea			Lethargy			Irritability			Loss of appetite		
			All Grades (1,2,3)			Grades 2 or 3	All Grades (1,2,3)			All Grades (1,2,3)			All Grades (1,2,3)			All Grades (1,2,3)			All Grades (1,2,3)		
		N	n	%	(95% CI)	n	n	%	(95% CI)	n	%	(95% CI)	n	%	(95% CI)	n	%	(95% CI)	n	%	(95% CI)
Primary	PsA-TT	201	8	4.0	(1.7-7.7)	2	1	0.5*	(0.0-2.7)	20	10.0	(6.2-14.9)	7	3.5	(1.4-7.0)	4	2.0	(0.5-5.0)	6	3.0	(1.1-6.4)
	PsACWY	200	6	3	(1.1-6.4)	1	7	3.5*	(1.4-7.1)	21	10.5	(6.6-15.6)	7	3.5	(1.4-7.1)	5	2.5	(0.8-5.7)	12	6	(3.1-10.2)
	Hib-TT	200	6	3	(1.1-6.4)	1	4	2	(0.5-5.0)	20	10	(6.2-15.0)	4	2	(0.5-5.0)	3	1.5	(0.3-4.3)	4	2	(0.5-5.0)
Booster	PsA-TT/PsA-TT	64	1	1.6	(0.0-8.4)	0	1	1.6	(0.0-8.4)	8	12.5	(5.6-23.2)	0	0	(0.0-5.6)	0	0	(0.0-5.6)	2	3.1	(0.4-10.8)
	PsA-TT/PsACWY	67	1	1.5	(0.0-8.0)	0	1	1.5	(0.0-8.0)	5	7.5	(2.5-16.6)	0	0	(0.0-5.4)	0	0	(0.0-5.4)	3	4.5	(0.9-12.5)
	PsA-TT/Hib-TT	66	0	0	(0.0-5.4)	0	1	1.5	(0.0-8.2)	3	4.5	(0.9-12.7)	0	0	(0.0-5.4)	0	0	(0.0-5.4)	0	0	(0.0-5.4)
	PsACWY/PsA-TT	65	1	1.5	(0.0-8.3)	1	2	3.1	(0.4-10.7)	4	6.2	(1.7-15.0)	0	0	(0.0-5.5)	0	0	(0.0-5.5)	3	4.6	(1.0-12.9)
	PsACWY/PsACWY	64	4	6.3	(1.7-15.2)	1	1	1.6	(0.0-8.4)	7	10.9	(4.5-21.2)	0	0	(0.0-5.6)	1	1.6	(0.0-8.4)	7	10.9	(4.5-21.2)
	PsACWY/Hib-TT	68	1	1.5	(0.0-7.9)	1	1	1.5	(0.0-7.9)	2	2.9	(0.4-10.2)	0	0	(0.0-5.3)	0	0	(0.0-5.3)	0	0	(0.0-5.3)
	Hib-TT/PsA-TT	63	2	3.2	(0.4-11.0)	0	1	1.6	(0.0-8.5)	8	12.7	(5.6-23.5)	1	1.6	(0.0-8.5)	1	1.6	(0.0-8.5)	3	4.8	(1.0-13.3)
	Hib-TT/PsACWY	66	0	0	(0.0-5.4)	0	0	0	(0.0-5.4)	5	7.6	(2.5-16.8)	0	0	(0.0-5.4)	0	0	(0.0-5.4)	2	3.0	(0.4-10.5)
	Hib-TT/Hib-TT	66	2	3.0	(0.4-10.5)	1	0	0	(0.0-5.4)	6	9.1	(3.4-18.7)	0	0	(0.0-5.4)	0	0	(0.0-5.4)	2	3.0	(0.4-10.5)

* P = 0.0370 for the comparison of PsACWY vs. PsA-TT using Fisher's exact test.

No Grade 3 Fever was reported. The severity of other systemic reactions was not assessed in this study.

Supplementary Appendix Table 7b. Proportion of subjects with systemic postimmunization reactions for study B conducted in healthy 2- to 29-year-olds

Age group	Vaccine group		Fever				Vomiting				Diarrhea				Lethargy				Irritability				Loss of appetite		
			All Grades (1,2,3)			Grades 2 or 3	All Grades (1,2,3)				All Grades (1,2,3)				All Grades (1,2,3)				All Grades (1,2,3)				All Grades (1,2,3)		
		N	n	%	(95% CI)	n	n	%	(95% CI)		n	%	(95% CI)		n	%	(95% CI)		n	%	(95% CI)		n	%	(95% CI)
2-10 yrs	PsA-TT	203	7	3.4	(1.4-7.0)	0	4	2.0	(0.5-5.0)		4	2.0	(0.5-5.0)		3	1.5	(0.3-4.3)		0	0	(0.0-1.8)		1	0.5	(0.0-2.7)
	PsACWY	99	2	2.0	(0.2-7.1)	0	3	3.0	(0.6-8.6)		0	0	(0.0-3.7)		2	2.0	(0.2-7.1)		1	1.0	(0.0-5.5)		1	1.0	(0.0-5.5)
11-17 yrs	PsA-TT	202	6	3.0	(1.1-6.4)	0	1	0.5	(0.0-2.7)		2	1.0	(0.1-3.5)												
	PsACWY	99	1	1.0	(0.0-5.5)	0	1	1.0	(0.0-5.5)		1	1.0	(0.0-5.5)												
18-29 yrs	PsA-TT	199	5	2.5	(0.8-5.8)	1	3	1.5	(0.3-4.3)		0	0	(0.0-1.8)												
	PsACWY	98	2	2.0	(0.2-7.2)	0	1	1.0	(0.0-5.6)		1	1.0	(0.0-5.6)												
Total	PsA-TT	604	18	3.0	(1.8-4.7)	1	8	1.3	(0.6-2.6)		6	1.0	(0.4-2.1)												
	PsACWY	296	5	1.7	(0.6-3.9)	0	5	1.7	(0.6-3.9)		2	0.7	(0.1-2.4)												

			Headache				Fatigue				Myalgia				Arthralgia		
			All Grades (1,2,3)			Grades 2 or 3	All Grades (1,2,3)				All Grades (1,2,3)				All Grades (1,2,3)		
		N	n	%	(95% CI)	n	n	%	(95% CI)		n	%	(95% CI)		n	%	(95% CI)
2-10 yrs	PsA-TT																
	PsACWY																
11-17 yrs	PsA-TT	202	21	10.4	(6.6-15.5)	1	1	0.5	(0.0-2.7)		1	0.5	(0.0-2.7)		1	0.5	(0.0-2.7)
	PsACWY	99	8	8.1	(3.6-15.3)	0	4	4.0	(1.1-10.0)		0	0	(0.0-3.7)		1	1.0	(0.0-5.5)
18-29 yrs	PsA-TT	199	24	12.1	(7.9-17.4)	0	5	2.5	(0.8-5.8)		2	1.0	(0.1-3.6)		1	0.5	(0.0-2.8)
	PsACWY	98	13	13.3	(7.3-21.6)	2	6	6.1	(2.3-12.9)		3	3.1	(0.6-8.7)		2	2.0	(0.2-7.2)
Total	PsA-TT	401	45	11.2	(8.3-14.7)	1	6	1.5*	(0.6-3.2)		3	0.7	(0.2-2.2)		2	0.5	(0.1-1.8)
	PsACWY	197	21	10.7	(6.7-15.8)	2	10	5.1*	(2.5-9.1)		3	1.5	(0.3-4.4)		3	1.5	(0.3-4.4)

* P = 0.0108 for the comparison of PsACWY vs. PsA-TT using CMH test adjusting for age group.

No Grade 3 Fever and Headache were reported. Neither Grade 2 nor Grade 3 reactions were reported for any of the other eight systemic reactions.

d. Supplementary Appendix Table 8. Proportion of subjects with adverse events (AEs) 28 days after vaccination for study A and study B

The severity of the AEs identified was assessed using the following intensity grade parameters:
1 Discomfort noted, but no disruption of normal daily activities; slightly bothersome; relieved with or without symptomatic treatment.
2 Discomfort sufficient to reduce or affect normal daily activity to some degree; bothersome; interferes with activities, only partially relieved with symptomatic treatment.
3 Discomfort sufficient to reduce or affect normal daily activity considerably (prevents regular activities for at least 24 hours); not relieved with symptomatic treatment, would cause subject or parent/legal guardian to seek medical advice.

Supplementary Appendix Table 8a. Number of AEs for study A conducted in healthy 12- to 23-month-olds

Primary System Organ Class Term			Infections and infestations	Respiratory, thoracic and mediastinal disorders	Gastrointestinal disorders	Eye disorders	Skin and subcutaneous tissue disorders	General disorders and administration site conditions	Injury, poisoning and procedural complications	Blood and lymphatic system disorders	Cardiac disorders	ALL
Immunization (AE Grades)	**Vaccine group**	**N**	**n**	**n**	**n**				**n**		**n**	**n**
Primary	PsA-TT	201	64	12	9	6	4	1	0	0	0	**96**
All Grades (1,2,3)	PsACWY	200	57	11	5	5	4	2	1	0	1	**86**
	Hib-TT	200	51	15	4	4	4	1	2	0	0	**81**
Grades 2 or 3	PsA-TT	201	9	0	2	0	0	0	0	0	0	**11**
	PsACWY	200	9	0	0	0	0	0	0	0	0	**9**
	Hib-TT	200	11	1	0	0	0	0	2	0	0	**14**
Booster	PsA-TT/PsA-TT	64	4	0	0	0	0	0	0	0	0	**4**
All Grades (1,2,3)	PsA-TT/PsACWY	67	3	0	1	0	1	0	0	0	0	**5**
	PsA-TT/Hib-TT	66	5	0	0	0	0	0	0	0	0	**5**
	PsACWY/PsA-TT	65	7	0	0	0	0	0	0	0	0	**7**
	PsACWY/PsACWY	64	6	0	0	0	0	0	0	0	0	**6**
	PsACWY/Hib-TT	68	7	0	0	0	1	0	0	0	0	**8**
	Hib-TT/PsA-TT	63	4	0	0	0	0	0	1	1	0	**6**
	Hib-TT/PsACWY	66	10	1	0	0	0	0	0	1	0	**12**
	Hib-TT/Hib-TT	66	5	2	1	0	0	0	0	0	0	**8**
Grades 2 or 3	PsA-TT/PsA-TT	64	0	0	0	0	0	0	0	0	0	**0**
	PsA-TT/PsACWY	67	1	0	1	0	0	0	0	0	0	**2**
	PsA-TT/Hib-TT	66	1	0	0	0	0	0	0	0	0	**1**
	PsACWY/PsA-TT	65	2	0	0	0	0	0	0	0	0	**2**
	PsACWY/PsACWY	64	2	0	0	0	0	0	0	0	0	**2**
	PsACWY/Hib-TT	68	3	0	0	0	0	0	0	0	0	**3**
	Hib-TT/PsA-TT	63	2	0	0	0	0	0	0	1	0	**3**
	Hib-TT/PsACWY	66	3	0	0	0	0	0	0	0	0	**3**
	Hib-TT/Hib-TT	66	0	1	0	0	0	0	0	0	0	**1**
Number of AEs			**252**	**42**	**22**	**15**	**14**	**4**	**6**	**2**	**1**	**358**
Percentage of the TOTAL number of AEs reported			70.4%	11.7%	6.1%	4.2%	3.9%	1.1%	1.7%	0.6%	0.3%	**100.0%**
Number of subjects with ≥ 1 AE reported			**163**	**38**	**20**	**15**	**14**	**4**	**4**	**2**	**1**	**218***
Percentage of subjects with ≥ 1 AE reported†			27.1%	6.3%	3.3%	2.5%	2.3%	0.7%	0.7%	0.3%	0.2%	**36.3%**

Adverse events reported in this table do not include local and systemic reactions ongoing beyond 4 days postimmunization.

* 218 is the overall number of subjects with ≥ 1 AE reported. It is less than the sum of the number of subjects with ≥ 1 AE reported in each primary System Organ Class category because some subjects reported multiple AEs under different categories.

† Percent denominator is 601, the total number of subjects vaccinated.

For primary immunization, 2 Grade 3 AEs (malaria and respiratory infection) were reported on the same subject in PsACWY group; the subject recovered without sequelae within 12 days. No other Grade 3 AEs were reported.

Supplementary Appendix Table 8b. Number of AEs for study B conducted in healthy 2- to 29-year-olds

Primary System Organ Class Term			Infections and infestations	Gastrointestinal disorders	Respiratory, thoracic and mediastinal disorders	Nervous system disorders	General disorders and administration site conditions	Blood and lymphatic system disorders	Muskuloskeletal and connective tissue disorders	ALL
Immunization (AE Grades)	**Vaccine group**	**N**	**n**	**n**	**n**	**n**			**n**	**n**
Primary	PsA-TT	604	54	5	3	1	1	1	0	**65**
All Grades (1,2,3)	PsACWY	296	26	3	0	1	0	0	1	**31**
Grades 2 or 3	PsA-TT	604	10	1	0	0	0	0	0	**11**
	PsACWY	296	6	0	0	0	0	0	1	**7**
Number of AEs (All Grades)			**80**	**8**	**3**	**2**	**1**	**1**	**1**	**96**
Percentage of the TOTAL number of AEs reported			83.3%	8.3%	3.1%	2.1%	1.0%	1.0%	1.0%	**100.0%**
Number of subjects with ≥ 1 AE reported			**72**	**8**	**3**	**2**	**1**	**1**	**1**	**84***
Percentage of subjects with ≥ 1 AE reported†			8.0%	0.9%	0.3%	0.2%	0.1%	0.1%	0.1%	**9.3%**

Adverse events reported in this table do not include local and systemic reactions ongoing beyond 4 days postimmunization.

* 84 is the overall number of subjects with ≥ 1 AE reported. It is less than the sum of the number of subjects with ≥ 1 AE reported in each primary System Organ Class category because some subjects reported multiple AEs under different categories.

† Percent denominator is 900, the total number of subjects vaccinated.

No Grade 3 AEs were reported.

e. *Supplementary Appendix Table 9. Proportion of subjects with serious adverse events (SAEs) after vaccination for study A and study B*

Supplementary Appendix Table 9a. Number of SAEs for study A conducted in healthy 12- to 23-month-olds

Primary System Organ Class Term			Infections and infestations	Gastrointestinal disorders	Injury, poisoning and procedural complications	Metabolism and nutrition disorders	Vascular disorders	ALL
Immunization	**Vaccine group**	**N**	**n**	**n**	**n**	**n**	**n**	**n**
Primary	PsA-TT	201	2	0	0	1	0	**3**
	PsACWY	200	2	2	1	0	0	**5**
	Hib-TT *	200	2	0	0	0	0	**2**
Booster	PsA-TT/PsA-TT	64	0	0	0	0	0	**0**
	PsA-TT/PsACWY	67	0	0	0	1	0	**1**
	PsA-TT/Hib-TT	66	0	0	0	0	0	**0**
	PsACWY/PsA-TT	65	1	0	0	0	1	**2**
	PsACWY/PsACWY	64	1	0	0	0	0	**1**
	PsACWY/Hib-TT	68	1	0	0	0	0	**1**
	Hib-TT/PsA-TT	63	0	0	0	0	0	**0**
	Hib-TT/PsACWY	66	0	0	0	0	0	**0**
	Hib-TT/Hib-TT	66	0	0	1	0	0	**1**
Number of SAEs			**9**	**2**	**2**	**2**	**1**	**16**
Percentage of the TOTAL number of SAEs reported			56.3%	12.5%	12.5%	12.5%	6.3%	**100.0%**
Number of subjects with ≥ 1 SAE reported			**8**	**2**	**2**	**2**	**1**	**15**
Percentage of subjects with ≥ 1 SAE reported†			1.3%	0.3%	0.3%	0.3%	0.2%	**2.5%**

SAEs presented in this table were reported over the 2 years of the entire study period, 10 months postprimary immunization plus 14 months postbooster immunization.

* Two SAEs were reported for the same subject in the Hib-TT group (two cases of bronchopneumonia 106 and 272 days respectively after vaccination).

† Percent denominator is 601, the total number of subjects vaccinated.

Note: Five cases of SAEs resulted in death. Two of them occurred postprimary immunization: protein energy malnutrition and acute gastroenteritis 226 and 250 days postimmunization in the PsA-TT group. Three of them occurred post-booster immunization: complication of marasmus 42 days postimmunization in the PsA-TT/PsACWY group and both cerebral malaria 356 days postimmunization and haemorrhage from internal injuries due to car accident 398 days postimmunization in the PsACWY/PsA-TT group.

Supplementary Appendix Table 9b. Number of SAEs for study B conducted in healthy 2- to 29-year-olds

Primary System Organ Class Term			Infections and infestations	Gastrointestinal disorders	Injury, poisoning and procedural complications	Pregnancy, puerperium and perinatal conditions	ALL
Immunization	**Vaccine group**	**N**	**n**	**n**	**n**	**n**	**n**
Primary	PsA-TT	604	0	0	1	1	**2**
	PsACWY	296	1	1	0	1	**3**
Number of SAEs			**1**	**1**	**1**	**2**	**5**
Percentage of the TOTAL number of SAEs reported			20.0%	20.0%	20.0%	40.0%	**100.0%**
Number of subjects with ≥ 1 SAE reported			**1**	**1**	**1**	**2**	**5**
Percentage of subjects with ≥ 1 SAE reported†			0.1%	0.1%	0.1%	0.2%	**0.6%**

SAEs presented in this table were reported over the 1 year of the entire study period.

† Percent denominator is 900, the total number of subjects vaccinated.

Note: No case of SAE resulted in death.

f. Supplementary Appendix Table 10. Etiology of the serious adverse events (SAEs) after vaccination for study A and study B, summarized by system organ class and preferred term

Supplementary Appendix Table 10a. Etiology of the SAEs (preferred term) for study A conducted in healthy 12- to 23-month-olds

Primary System Organ Class Term			Infections and infestations	Gastrointestinal disorders	Injury, poisoning and procedural complications	Metabolism and nutrition disorders	Vascular disorders	ALL
Immunization	**Vaccine group**	**N**	**Preferred Term (n)**	**Preferred Term (n)**	**Preferred Term (n)**	**Preferred Term (n)**	**Preferred Term (n)**	**n**
Primary	PsA-TT	201	Bronchopneumonia (1) Gastroenteritis (1), RESULTED IN DEATH	NA (0)	NA (0)	Kwashiorkor (1), RESULTED IN DEATH	NA (0)	**3**
	PsACWY	200	Lower respiratory tract infection (1) Bronchopneumonia (1)	Umbilical hernia, obstructive (1) Food poisoning (1)	Thermal burns (1)	NA (0)	NA (0)	**5**
	Hib-TT	200	Bronchopneumonia (2)*	NA (0)	NA (0)	NA (0)	NA (0)	**2**
Booster	PsA-TT/PsA-TT	64	NA (0)	NA (0)	NA (0)	NA (0)	NA (0)	**0**
	PsA-TT/PsACWY	67	NA (0)	NA (0)	NA (0)	Marasmus (1), RESULTED IN DEATH	0	**1**
	PsA-TT/Hib-TT	66	NA (0)	NA (0)	NA (0)	NA (0)	NA (0)	**0**
	PsACWY/PsA-TT	65	Cerebral malaria (1), RESULTED IN DEATH	NA (0)	NA (0)	NA (0)	Traumatic haemorrhage (1), RESULTED IN DEATH	**2**
	PsACWY/PsACWY	64	Meningitis meningococcal (1)†	NA (0)	NA (0)	NA (0)	NA (0)	**1**
	PsACWY/Hib-TT	68	Cerebral malaria (1)	NA (0)	NA (0)	NA (0)	NA (0)	**1**
	Hib-TT/PsA-TT	63	NA (0)	NA (0)	NA (0)	NA (0)	NA (0)	**0**
	Hib-TT/PsACWY	66	NA (0)	NA (0)	NA (0)	NA (0)	NA (0)	**0**
	Hib-TT/Hib-TT	66	NA (0)	NA (0)	Femur fracture (1)	NA (0)	NA (0)	**1**
Number of SAEs			**9**	**2**	**2**	**2**	**1**	**16**

SAEs presented in this table were reported over the 2 years of the entire study period, none of them were vaccine-related events.

NA = Not Applicable (no case of SAE in this cell).

* Two SAEs were reported for the same subject in the Hib-TT group (two cases of bronchopneumonia 106 and 272 days respectively after vaccination).

† A case of meningococcal A meningitis, which occurred in Mali at the end of the 2008 dry season in a 2-year-old male subject. The subject was promptly treated and recovered without sequelae. Serologic results subsequently revealed that the subject had responded to a primary vaccination with the PsACWY vaccine, but the immune response waned rapidly to preimmunization antibody levels. The subject later responded to a second dose of reduced PsACWY vaccine (1/5th), but again the immune response waned rapidly to preimmunization antibody levels, with no evidence of an anamnestic response.

Supplementary Appendix Table 10b. Etiology of the SAEs (preferred term) for study B conducted in healthy 2- to 29-year-olds

Primary System Organ Class Term			Infections and infestations	Gastrointestinal disorders	Injury, poisoning and procedural complications	Pregnancy, puerperium and perinatal conditions	ALL
Immunization	**Vaccine group**	**N**	**Preferred Term (n)**	**Preferred Term (n)**	**Preferred Term (n)**	**Preferred Term (n)**	**n**
Primary	PsA-TT	604	NA (0)	NA (0)	Spinal cord injury, lumbar (1)	Stillbirth (1)*	**2**
	PsACWY	296	Pyelonephritis (1)	Umbilical hernia, obstructive (1)	NA (0)	Preeclampsia (1)	**3**
Number of SAEs			**1**	**1**	**1**	**2**	**5**

SAEs presented in this table were reported over the 1 year of the entire study period, none of them were vaccine-related events.

NA = Not Applicable (no case of SAE in this cell).

* A case of a stillborn with no congenital anomaly or birth defect, delivered 13 month after vaccination to a 26 year-old woman who had obstructed labour with a previous history of still births.

Note: No case of SAE resulted in death.

8. Conferences specific abstracts references

Preliminary results of the data contained in this paper were presented to the following scientific meetings and conferences.

Conference of the 100yr of the Royal Society of Hygiene and Tropical Medicine, 12-13 September 2007, London, UK. Samba Sow, Brown Okoko, Marie-Pierre Preziosi, Elisa Marchetti, Milagritos Tapia, Richard Adegbola, Ray Borrow, George Carlone, Fadima Cheick Haidara, Adebayo Akinsola, Souleymane Diakité, Varsha Parulekar, Brian Plikaytis, Helen Findlow, Cheryl Elie, Jean-Marie Préaud, Subash Kapre, Suresh Jadav, Marc LaForce, Prasad Kulkarni and Simonetta Viviani. A Phase II, Observer Blind, Randomized Study to Evaluate the Safety and Immunogenicity a New Meningococcal Group A Conjugate Vaccine in Healthy African Toddlers Residing in the Meningitis Belt. [Poster]

56th Annual Meeting of the American Society of Tropical Medicine and Hygiene, November 4-8, 2007, Philadelphia, PA, USA. Sow SO, Brown O, Preziosi MP, Marchetti E, Tapia MD, Haidara FC, Adegbola R, Borrow R, Carlone G, Akinsola A, Diakite S, Parulekar V, Plikaytis B, Findlow H, Elie C, Preaud J, Kapre S, Jadav S, LaForce M, Kulkarni P, Viviani S. A Phase II Vaccine Trial of Meningococcal A Conjugate Vaccine (PsATT) in African Toddlers. [Poster]

57th Annual Meeting of the American Society of Tropical Medicine and Hygiene, December 7-11, 2008, New Orleans, LA, USA. Olubukola T. Idoko, Brown J. Okoko, Samba Sow, Milagritos Tapia, Marie-Pierre Preziosi, Elisa Marchetti, Fadima C. Haidara, Lionel Martellet, Julie Chaumont, Varsha Parulekar, Brian Plikaytis, Ray Borrow, George Carlone, Richard Adegbola, Jean-Marie Preaud, Prasad Kulkarni, Subhash Kapre, Suresh Jadhav, Musa Hassan-King, Marc LaForce, Simonetta Viviani, Helen Findlow, Cheryl Elie. A Phase II, Observer Blind, Randomized, Controlled Study to Evaluate the Safety, Immunogenicity and Immunological Memory of a Booster dose of a New Group A Meningococcal ConjugateVaccine (MenAfriVa c ™) in Healthy African Children Previously Primed at 12-23 months of age. [Poster]

57th Annual Meeting of the American Society of Tropical Medicine and Hygiene, December 7-11, 2008, New Orleans, LA, USA. Fadima Cheick Haidara , Brown J Okoko, Milagritos Tapia, Fatoumata Diallo, Rokiatou Dembele, Samba Sow, Richard Adegbola, Marie-Pierre Preziosi, Elisa Marchetti, Olubukola Idoko, Awa Traore Dembele, Julie Chaumont, Varsha Parulekar, Brian Plikaytis, Helen Findlow, Cheryl Elie, Ray Borrow, George Carlone, Prasad Kulkarni, Musa Hassan-King, Marc LaForce, Simonetta Viviani. Safety and Immunogenicity of a new Meningococcal A conjugate vaccine in a healthy African population aged 2-29 years. [Poster]

IDSA (Infectious Diseases Society of America) 45th Annual Meeting. October 4-7, 2007, San Diego, Ca, USA. M. C. Bash, S. Sow, B. Okoko, M. Preziosi, E. Marchetti, M. Tapia, R. Adegbola, F. C. Haidara, A. Akinsola, R. Borrow, G. Carlone, P. Kulkarni, M. Hassan-King, M. LaForce, S. Viviani. A Phase II Safety and Immunogenicity Study of a New Meningococcal Group A Conjugate Vaccine in Healthy African Toddlers Residing in the Meningitis Belt. [Poster]

16th International Pathogenic Neisseria Conference, 7-12 September 2008, Rotterdam, The Netherlands. Brown Okoko, Samba Sow, Milagritos Tapia, Richard Adegbola, Marie-Pierre Preziosi, Elisa Marchetti, Fadima Cheick Haidara, Idoko Olubukola , Lionel Martellet , Julie Chaumont , Varsha Parulekar, Brian Plikaytis, Helen Findlow, Cheryl Elie, Ray Borrow, George Carlone, Jean-Marie Préaud, Prasad Kulkarni, Subhash Kapre , Suresh Jadhav, Musa Hassan-King, Marc LaForce, Simonetta Viviani. A Phase II, Observer Blind, Randomized, Controlled Study to Evaluate the Safety, Immunogenicity and Immunological Memory of a Booster dose of a New Group A Meningococcal Conjugate Vaccine (MenAfriVac (tm)) in Healthy African Children Previously Primed at 12-23 months of age. [Poster]

16th International Pathogenic Neisseria Conference, 7-12 September 2008, Rotterdam, The Netherlands. Aldiouma Diallo, Samba Sow, Brown Okoko, Pascal Arduin, Fadima Cheikh Haidara, Milagritos Tapia, Olubukola Idoko, Richard Adegbola, Marie-Pierre Preziosi, Elisa Marchetti, Julie Chaumont, Kader Konde, Jamie Findlow, Cheryl Elie, Varsha Parulekar, Brian Plikaytis, Ray Borrow, George Carlone, Prasad Kulkarni, Marc LaForce and Simonetta Viviani. Safety and Immunogenicity of a new Meningococcal A conjugate vaccine in a healthy African population aged 2-29 years. [Poster]