

Figure 1

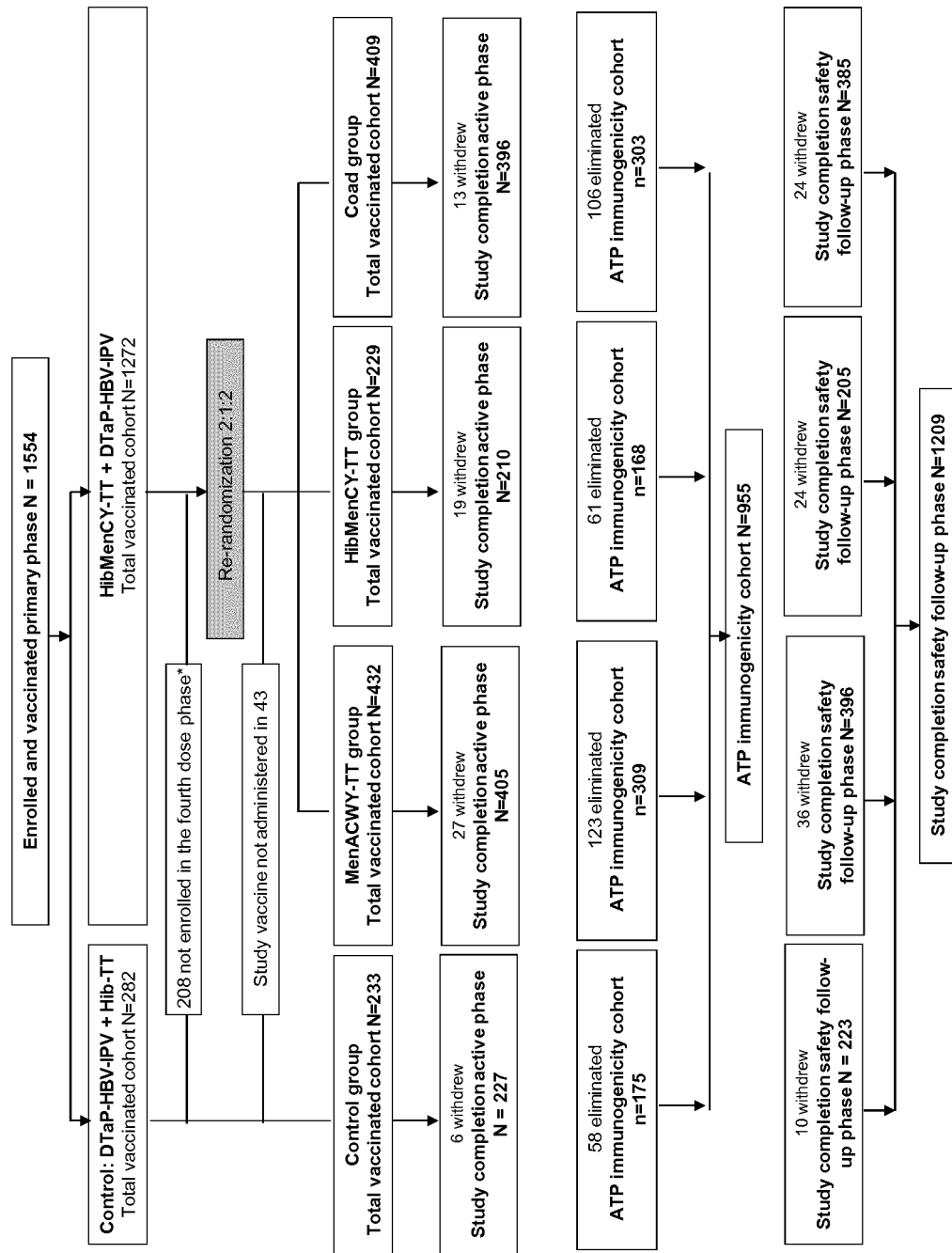


Figure 2

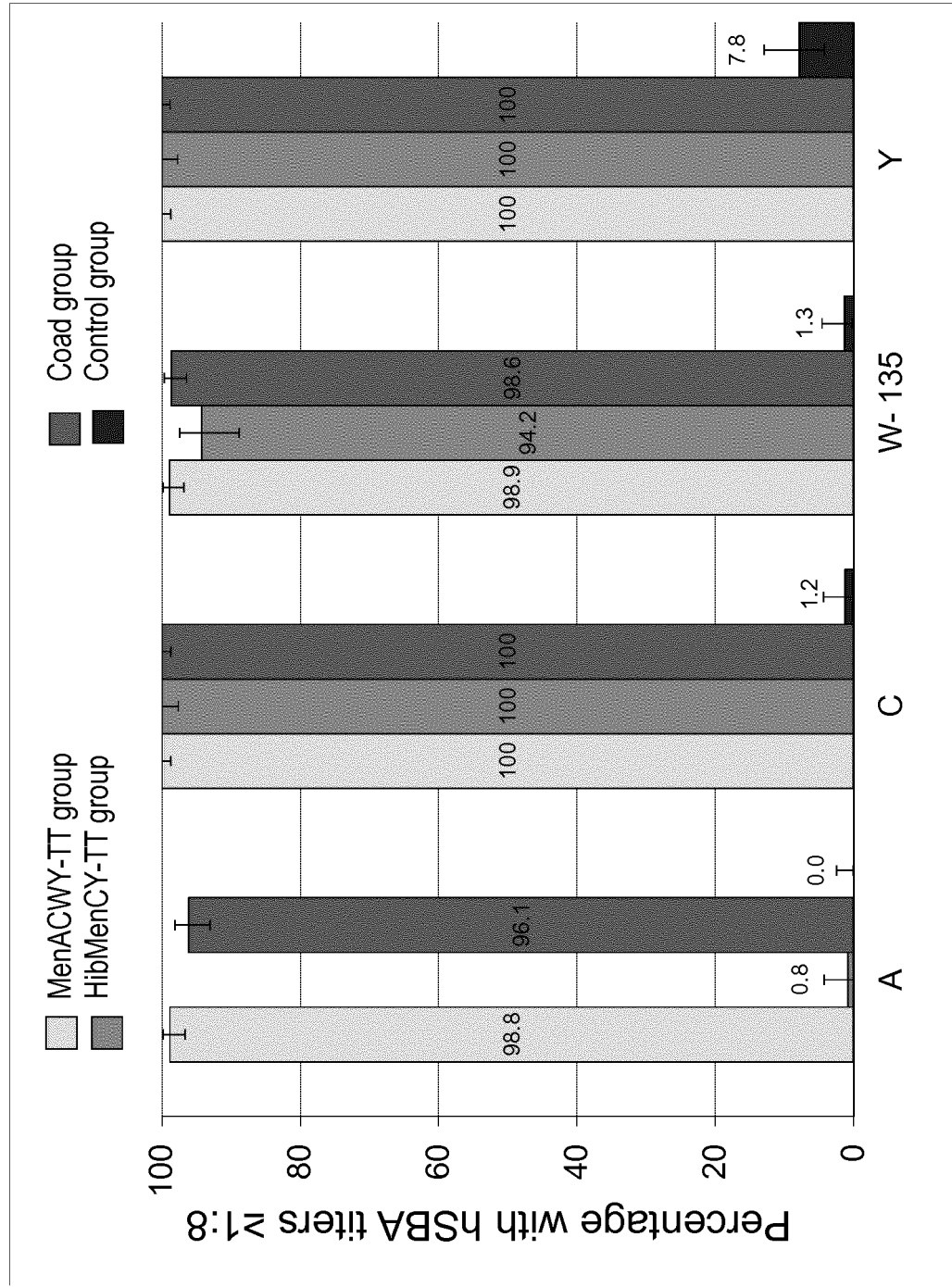


Figure 3

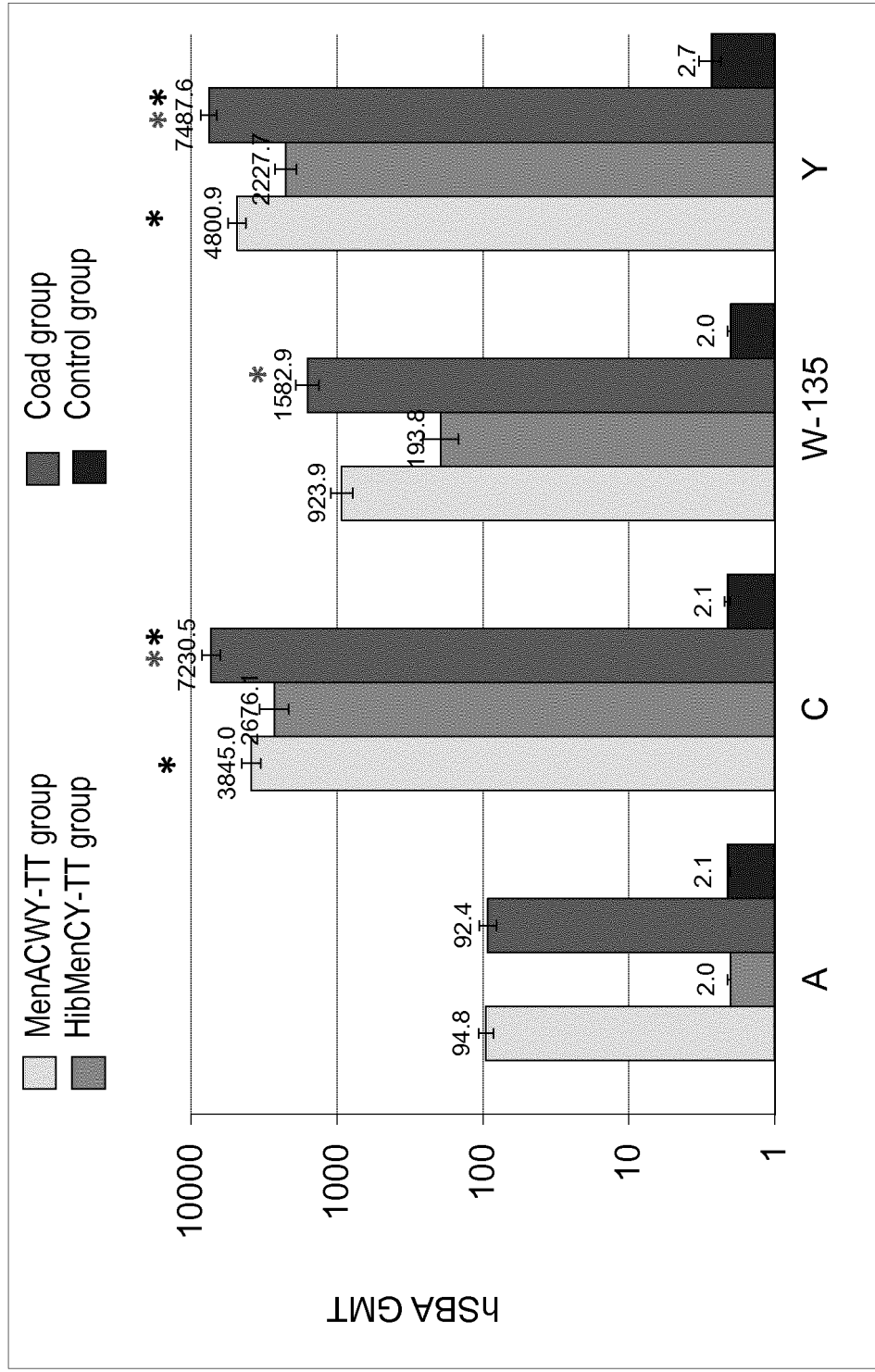


Figure 4

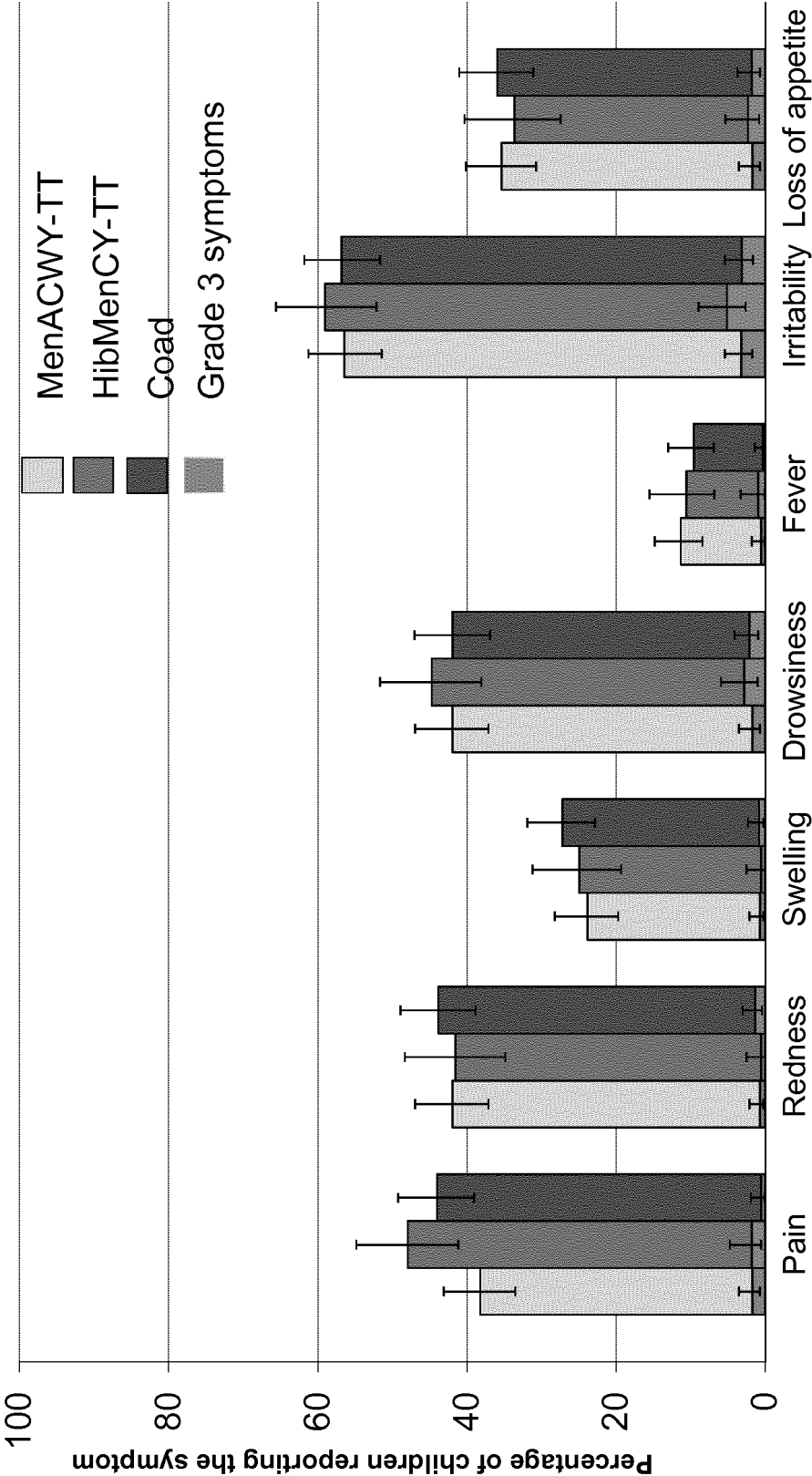


Table 1 Study design

Group name	Primary phase vaccination*	Fourth dose phase vaccination*				
	(Visits 1-4)	12-15 months (Visit 4)	1 month post vaccination (Visit 5)	15-18 months (Visit 6)	1 month post vaccination (Visit 7)	
2, 4, 6 months		Vaccination	Blood sampling	Blood sampling	Vaccination	Blood sampling
MenACWY-TT	HibMenCY-TT + DTaP-HBV-IPV	MenACWY-TT	Yes	-	DTaP	Yes
HibMenCY-TT	HibMenCY-TT + DTaP-HBV-IPV	HibMenCY-TT	Yes	-	DTaP	Yes
Coad	HibMenCY-TT + DTaP-HBV-IPV	No vaccination	-	Yes	MenACWY-TT + DTaP	Yes
Control	Hib-TT + DTaP-HBV-IPV	No vaccination	-	-	DTaP	Yes

Shaded areas indicate vaccination and blood sampling time points discussed in the present report. * All subjects were permitted to receive routine vaccines recommended by the

Advisory Committee on Immunization Practices. For measles, mumps, rubella, varicella, hepatitis A and Hib vaccines, vaccination was to occur ≥ 30 days before or after administration of study vaccines. A shortage of Hib conjugate vaccine in the US at the time of the study led ACIP to recommend deferral of the booster dose of Hib for all toddlers to allow Hib conjugate vaccine to be preferentially administered to infants, who are at the highest risk of invasive Hib disease. In compliance with this recommendation, Hib boosters were not administered to anyone except those in the HibMenCY-TT group. Other groups were to receive the fourth dose of Hib conjugate vaccine when the shortage was resolved.

Table 2 Results of the inferential analysis for meningococcal antigens administered at 12-15 or 15-18 months of age (Primary objectives: ATP immunogenicity cohort, Fourth dose phase).

Objective	Endpoint	Criteria	Serogroup	Value	[95% CI]	Criterion met?
Non-inferiority MenACWY-TT vs HibMenCY-TT	hSBA titers $\geq 1:8$	LL of 2-sided 95% CI for difference (MenACWY-TT - HibMenCY-TT) is $\geq -10\%$	C	0.0	[-1.33; 2.42]	Yes
			Y	0.0	[-1.31; 2.39]	Yes
Immunogenicity of MenACWY-TT		LL of 2-sided 95% CI is $\geq 80\%$	A	98.8	[96.6; 99.8]	Yes
			W-135	98.9	[96.8; 99.8]	Yes
Non-inferiority Coad vs HibMenCY-TT	hSBA titers $\geq 1:8$	LL of 2-sided 95% CI for difference (Coad -HibMenCY-TT) is $\geq -10\%$	C	0.0	[-1.30; 2.42]	Yes
			Y	0.0	[-1.25; 2.39]	Yes
Immunogenicity of MenACWY-TT + DTaP		LL of 2-sided 95% CI (Coad group) is $\geq 80\%$	A	96.1	[93.0; 98.1]	Yes
			W-135	98.6	[96.4; 99.6]	Yes
Non-inferiority MenACWY-TT vs HibMenCY-TT	hSBA GMT ratio	LL of 95%CI for ratio (MenACWY / HibMenCY-TT) is ≥ 0.5	C	1.44	[1.11; 1.87]	Yes*
			Y	2.16	[1.71; 2.71]	Yes*
Non-inferiority Coad vs HibMenCY-TT		LL of 2-sided 95% CI for ratio (Coad /HibMenCY-TT) is ≥ 0.5	C	2.70	[2.08; 3.50]	Yes*
			Y	3.36	[2.72; 4.15]	Yes*

95% CI – 95 percent confidence interval; LL– lower limit of the 95% CI; GMT – geometric mean antibody titer, ATP – according to protocol. *The primary objectives were concluded in a hierarchical manner. One of the non-inferiority criteria for co-administration objectives related to pertussis vaccination (reported elsewhere) was not met. Therefore for subsequent objectives (indicated above by *), non-inferiority could not be concluded as met even though the pre-specified criterion was met.

Table 3 (Supplementary): Details of the reasons why subjects withdrew from the study or were eliminated from the According to Protocol (ATP) cohort.

	Group			
	Control	MenACWY-TT	HibMenCY-TT	Coad
Withdrawals from study completion active phase	6 withdrew: lost to follow-up (5), other (1).	27 withdrew: adverse event (1), protocol violation (2), consent withdrawal (4); moved from study area (3), lost to follow up (14), other (3).	19 withdrew: serious adverse event (1), protocol violation (3), consent withdrawal (3); lost to follow-up (10), other (2).	13 withdrew: consent withdrawal (4), lost to follow up (8), other (1).
Withdrawals from study completion extended safety follow up phase	10 withdrew: consent withdrawal (1), lost to follow-up (9)	36 withdrew: consent withdrawal (7), lost to follow up (29)	24 withdrew: consent withdrawal (2), lost to follow-up (22)	24 withdrew: consent withdrawal (3), lost to follow up (21)
Eliminated from ATP immunogenicity cohort	58 eliminated: received forbidden vaccine (3), ineligible (4), eliminated during the primary phase (16), non-compliant with blood sampling (12), serology data missing (23)	123 eliminated: received forbidden vaccine (17), randomization failure (6), ineligible (13), eliminated during the primary phase (27), non-compliant with blood sampling (38), serology data missing (22)	61 eliminated: received forbidden vaccine (10), ineligible (4), eliminated during the primary phase (18), non-compliant with blood sampling (20), serology data missing (9)	106 eliminated: received forbidden vaccine (4), ineligible (4), eliminated during the primary phase (34), non-compliant with blood sampling (21), serology data missing (43)

Table 4 (Supplementary): Summary of demographic characteristics (ATP immunogenicity cohort, Fourth dose phase)

Characteristic		MenACWY-TT N = 309	HibMenCY-TT N = 168	Coad N = 303	Control N = 175
Age at Visit 6	Mean (SD)	15.2 (0.53)	15.3 (0.54)	15.3 (0.60)	15.3 (0.64)
(months)	Range	15-18	15-17	15-18	15-18
Gender	Female n(%)	150 (48.5)	86 (51.2)	138 (45.5)	97 (55.4)
	Male n(%)	159 (51.5)	82 (48.8)	165 (54.5)	78 (44.6)
Race	African/African American n(%)	33 (10.7)	19 (11.3)	15 (5.0)	8 (4.6)
	American Indian/Alaskan Native n(%)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
	Central/South Asian n(%)	1 (0.3)	0 (0.0)	1 (0.3)	0 (0.0)
	East Asian n(%)	1 (0.3)	1 (0.6)	1 (0.3)	1 (0.6)
	Japanese n(%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
	South East Asian n(%)	1 (0.3)	1 (0.6)	2 (0.7)	0 (0.0)
	Native Hawaiian/Pacific Islander n(%)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
	Arabic/North African n(%)	5 (1.6)	0 (0.0)	4 (1.3)	3 (1.7)
	Caucasian/European n(%)	243 (78.6)	130 (77.4)	251 (82.8)	144 (82.3)
	Other n(%)	24 (7.8)	16 (9.5)	29 (9.6)	18 (10.3)

N = total number of subjects

n/% = number / percentage of subjects in a given category

SD = standard deviation

ATP = according to protocol

Table 5: Percentage of subjects reporting specific adverse events from dose 1 up to 6 months after the fourth dose (Fourth Dose Total vaccinated cohort, primary and fourth dose phases)

	MenACWY-TT			HibMenCY-TT			Coad			Control		
	N = 432			N = 229			N = 409			N = 233		
	n	% (95% CI)		n	% (95% CI)		n	% (95% CI)		n	% (95% CI)	
At least one symptom	245	56.7 (51.9; 61.4)		140	61.1 (54.5; 67.5)		226	55.3 (50.3; 60.1)		105	45.1 (38.6; 51.7)	
SAE	30	6.9 (4.7; 9.8)		11	4.8 (2.4; 8.4)		26	6.4 (4.2; 9.2)		10	4.3 (2.1; 7.8)	
New onset chronic illness	67	15.5 (12.2; 19.3)		29	12.7 (8.6; 17.7)		66	16.1 (12.7; 20.1)		36	15.5 (11.1; 20.7)	
Drug hypersensitivity	12	2.8 (1.4; 4.8)		7	3.1 (1.2; 6.2)		9	2.2 (1.0; 4.1)		5	2.1 (0.7; 4.9)	
Food allergy	5	1.2 (0.4; 2.7)		1	0.4 (0.0; 2.4)		2	0.5 (0.1; 1.8)		2	0.9 (0.1; 3.1)	
Hypersensitivity	2	0.5 (0.1; 1.7)		0	0.0 (0.0; 1.6)		0	0.0 (0.0; 0.9)		1	0.4 (0.0; 2.4)	
Milk allergy	1	0.2 (0.0; 1.3)		0	0.0 (0.0; 1.6)		2	0.5 (0.1; 1.8)		1	0.4 (0.0; 2.4)	
Multiple allergies	2	0.5 (0.1; 1.7)		1	0.4 (0.0; 2.4)		2	0.5 (0.1; 1.8)		0	0.0 (0.0; 1.6)	
Seasonal allergy	3	0.7 (0.1; 2.0)		2	0.9 (0.1; 3.1)		2	0.5 (0.1; 1.8)		4	1.7 (0.5; 4.3)	
Selective IgA immunodeficiency	0	0.0 (0.0; 0.9)		0	0.0 (0.0; 1.6)		1	0.2 (0.0; 1.4)		0	0.0 (0.0; 1.6)	
Hypotonia	0	0.0 (0.0; 0.9)		0	0.0 (0.0; 1.6)		0	0.0 (0.0; 0.9)		1	0.4 (0.0; 2.4)	
Asthma	11	2.5 (1.3; 4.5)		2	0.9 (0.1; 3.1)		7	1.7 (0.7; 3.5)		3	1.3 (0.3; 3.7)	
Bronchial hyperreactivity	10	2.3 (1.1; 4.2)		4	1.7 (0.5; 4.4)		12	2.9 (1.5; 5.1)		5	2.1 (0.7; 4.9)	
Rhinitis allergic	4	0.9 (0.3; 2.4)		4	1.7 (0.5; 4.4)		6	1.5 (0.5; 3.2)		7	3.0 (1.2; 6.1)	
Alopecia areata	0	0.0; (0.0; 0.9)		1	0.4 (0.0; 2.4)		0	0.0 (0.0; 0.9)		0	0.0 (0.0; 1.6)	
Dermatitis allergic	3	0.7; (0.1; 2.0)		1	0.4 (0.0; 2.4)		0	0.0 (0.0; 0.9)		1	0.4 (0.0; 2.4)	
Dermatitis atopic	5	1.2; (0.4; 2.7)		0	0.0 (0.0; 1.6)		10	2.4 (1.2; 4.5)		2	0.9 (0.1; 3.1)	
Dermatitis contact	3	0.7; (0.1; 2.0)		1	0.4 (0.0; 2.4)		3	0.7 (0.2; 2.1)		1	0.4 (0.0; 2.4)	
Drug eruption	1	0.2; (0.0; 1.3)		0	0.0 (0.0; 1.6)		0	0.0 (0.0; 0.9)		0	0.0 (0.0; 1.6)	
Eczema	16	3.7; (2.1; 5.9)		7	3.1 (1.2; 6.2)		18	4.4 (2.6; 6.9)		6	2.6 (1.0; 5.5)	
Rash	1	0.2; (0.0; 1.3)		0	0.0 (0.0; 1.6)		0	0.0 (0.0; 0.9)		0	0.0 (0.0; 1.6)	

	MenACWY-TT			HibMenCY-TT			Coad			Control		
	N = 432			N = 229			N = 409			N = 233		
	n	% (95% CI)		n	% (95% CI)		n	% (95% CI)		n	% (95% CI)	
Rash*	120	27.8 (23.6; 32.3)		64	27.9 (22.2; 34.2)		106	25.9 (21.7; 30.5)		48	20.6 (15.6; 26.4)	
Emergency room visit	145	33.6 (29.1; 38.2)		92	40.2 (33.8; 46.8)		145	35.5 (30.8; 40.3)		57	24.5 (19.1; 30.5)	

At least one symptom = at least one symptom experienced (regardless of the MedDRA Primary System Organ Class)

N = number of subjects with at least one administered dose

n/% = number/percentage of subjects reporting the symptom at least once

95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

*from the fourth dose until 6 months after the fourth dose