Clinical trial results:
A Phase III Randomized, Partially Double-Blind, Active-Comparator-Controlled, Lot-to-Lot Consistency Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of V419 in Healthy Infants When Given at 2, 4, and 6 Months Concomitantly with Prevnar 13™ and RotaTeq™

Summary

EudraCT number	2011-004108-39
Trial protocol	Outside EU/EEA
Global end of trial date	26 July 2013

Results information

Result version number	v1 (current)
This version publication date	03 February 2016
First version publication date	17 July 2015

Trial information

Trial identification

Sponsor protocol code	V419-006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01340937
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp and Dohme Corp., A Subsidiary of Merck & Co., Inc.
Sponsor organisation address	2000 Galloping Hill Rd, Kenilworth, United States, 07033
Public contact	VP, Late Stage Development, Merck Sharp and Dohme Corp., A Subsidiary of Merck & Co., Inc., 800 672-6372, ClinicalTrialsDisclosure@merck.com
Scientific contact	VP, Late Stage Development, Merck Sharp and Dohme Corp., A Subsidiary of Merck & Co., Inc., 800 672-6372, ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000394-PIP01-08
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 July 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the consistency of the Postdose 3 immune response to three manufactured lots of PR5I when given at 2, 4, and 6 months of age with respect to geometric mean concentrations (GMCs) and geometric mean titers (GMTs).

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	11 May 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 2808
Worldwide total number of subjects	2808
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	2808

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled from 11 May 2011 to 26 July 2013 at 73 clinical sites in the United States.

Pre-assignment

Screening details:

A total of 2808 subjects met all of the inclusion criteria and were enrolled and randomized. Infant vaccinations were administered at 2, 4, and 6 months and the toddler vaccinations at 15 months of age. The Interim Period is the time between the last vaccination of the infant series and the time of administration of the toddler vaccination.

Period 1

Period 1 title	Infant Series
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Blinding implementation details:

This was a partially double-blind study (Investigator, study personnel, subject's parent(s), and personnel of the Sponsor) were blinded to the Lot A, B, or C of V419 the subject was randomized to receive but they were not blinded to the subject's vaccination group (V419 or Control).

Arms

Are arms mutually exclusive?	Yes
Arm title	V419 Lot A

Arm description:

V419 (Lot A) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.

Arm type	Experimental
Investigational medicinal product name	PR5I
Investigational medicinal product code	V419
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, and 6 months of age.

Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection at 15 months of age.

Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral, 1 dose each at 2, 4, and 6 months of age.

Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Arm title	V419 Lot B

Arm description:

V419 (Lot B) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.

Arm type	Experimental
Investigational medicinal product name	PR5I
Investigational medicinal product code	V419
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, and 6 months of age.

Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection at 15 months of age.

Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral, 1 dose each at 2, 4, and 6 months of age.

Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Arm title	V419 Lot C

Arm description:

V419 (Lot C) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.

Arm type	Experimental
Investigational medicinal product name	PR5I
Investigational medicinal product code	V419
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:	
0.5 mL, intramuscular, 1 injection each at 2, 4, and 6 months of age.	
Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL, intramuscular, 1 injection at 15 months of age.	
Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details:	
2 mL, oral, 1 dose each at 2, 4, and 6 months of age.	
Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.	
Arm title	Control
Arm description:	
PENTACEL™ 0.5 mL IM at 2, 4, 6, and 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age; and RECOMBIVAX HB™ 0.5 mL IM at 2 and 6 months of age.	
Arm type	Active comparator
Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.	
Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details:	
2 mL, oral, 1 dose each at 2, 4, and 6 months of age.	
Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.	

Investigational medicinal product name	RECOMBIVAX HB™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2 and 6 months of age.

Number of subjects in period 1	V419 Lot A	V419 Lot B	V419 Lot C
Started	800	797	809
Completed	742	737	753
Not completed	58	60	56
Physician decision	2	3	1
Consent withdrawn by subject	33	32	30
Adverse event, non-fatal	-	1	4
Death	2	-	2
Randomized but not vaccinated	-	5	2
Lost to follow-up	20	14	12
Protocol deviation	1	4	4
Other protocol criterion not met	-	1	1

Number of subjects in period 1	Control
Started	402
Completed	370
Not completed	32
Physician decision	-
Consent withdrawn by subject	15
Adverse event, non-fatal	-
Death	-
Randomized but not vaccinated	1
Lost to follow-up	13
Protocol deviation	3
Other protocol criterion not met	-

Period 2

Period 2 title	Interim Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Assessor

Blinding implementation details:

This was a partially double-blind study (Investigator, study personnel, subject's parent(s), and personnel of the Sponsor) were blinded to the Lot A, B, or C of V419 the subject was randomized to receive but they were not blinded to the subject's vaccination group (V419 or Control).

Arms

Are arms mutually exclusive?	Yes
Arm title	V419 Lot A

Arm description:

V419 (Lot A) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.

Arm type	Experimental
Investigational medicinal product name	PR5I
Investigational medicinal product code	V419
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, and 6 months of age.

Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection at 15 months of age.

Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral, 1 dose each at 2, 4, and 6 months of age.

Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Arm title	V419 Lot B

Arm description:

V419 (Lot B) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.

Arm type	Experimental

Investigational medicinal product name	PR5I
Investigational medicinal product code	V419
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, and 6 months of age.

Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral, 1 dose each at 2, 4, and 6 months of age.

Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection at 15 months of age.

Arm title	V419 Lot C

Arm description:

V419 (Lot C) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.

Arm type	Experimental
Investigational medicinal product name	PR5I
Investigational medicinal product code	V419
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, and 6 months of age.

Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral, 1 dose each at 2, 4, and 6 months of age.

Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection

Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection at 15 months of age.

Arm title	Control

Arm description:

PENTACEL™ 0.5 mL IM at 2, 4, 6, and 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age; and RECOMBIVAX HB™ 0.5 mL IM at 2 and 6 months of age.

Arm type	Active comparator
Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Investigational medicinal product name	RECOMBIVAX HB™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2 and 6 months of age.

Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral, 1 dose each at 2, 4, and 6 months of age.

Number of subjects in period 2	V419 Lot A	V419 Lot B	V419 Lot C
Started	742	737	753
Completed	675	658	669
Not completed	67	79	84
Consent withdrawn by subject	28	23	17
Physician decision	-	1	1
Adverse event, non-fatal	1	-	1
Lost to follow-up	29	48	53
Other technical problems	4	4	6
Protocol deviation	5	3	6

Number of subjects in period 2	Control
Started	370
Completed	329
Not completed	41
Consent withdrawn by subject	12
Physician decision	-
Adverse event, non-fatal	-
Lost to follow-up	23
Other technical problems	3
Protocol deviation	3

Period 3

Period 3 title	Toddler Vaccinations
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Assessor

Blinding implementation details:

This was a partially double-blind study (Investigator, study personnel, subject's parent(s), and personnel of the Sponsor) were blinded to the Lot A, B, or C of V419 the subject was randomized to receive but they were not blinded to the subject's vaccination group (V419 or Control).

Arms

Are arms mutually exclusive?	Yes
Arm title	V419 Lot A

Arm description:

V419 (Lot A) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.

Arm type	Experimental

Investigational medicinal product name	PR5I
Investigational medicinal product code	V419
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, and 6 months of age.

Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection at 15 months of age.

Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral, 1 dose each at 2, 4, and 6 months of age.

Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Arm title	V419 Lot B

Arm description:

V419 (Lot B) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.

Arm type	Experimental
Investigational medicinal product name	PR5I
Investigational medicinal product code	V419
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, and 6 months of age.

Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution

Routes of administration	Oral use
Dosage and administration details: 2 mL, oral, 1 dose each at 2, 4, and 6 months of age.	
Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: 0.5 mL, intramuscular, 1 injection at 15 months of age.	
Arm title	V419 Lot C
Arm description: V419 (Lot C) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Arm type	Experimental
Investigational medicinal product name	PR5I
Investigational medicinal product code	V419
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: 0.5 mL, intramuscular, 1 injection each at 2, 4, and 6 months of age.	
Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details: 2 mL, oral, 1 dose each at 2, 4, and 6 months of age.	
Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: 0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.	
Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: 0.5 mL, intramuscular, 1 injection at 15 months of age.	
Arm title	Control
Arm description: PENTACEL™ 0.5 mL IM at 2, 4, 6, and 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age; and RECOMBIVAX HB™ 0.5 mL IM at 2 and 6 months of age.	
Arm type	Active comparator

Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral, 1 dose each at 2, 4, and 6 months of age.

Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Investigational medicinal product name	RECOMBIVAX HB™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2 and 6 months of age.

Number of subjects in period 3	V419 Lot A	V419 Lot B	V419 Lot C
Started	675	658	669
Completed	666	641	660
Not completed	9	17	9
Consent withdrawn by subject	2	2	1
Lost to follow-up	6	14	7
Other technical problems	1	1	1
Protocol deviation	-	-	-

Number of subjects in period 3	Control
Started	329
Completed	319
Not completed	10
Consent withdrawn by subject	1
Lost to follow-up	8
Other technical problems	-

Protocol deviation	1

Period 4

Period 4 title	Combined Lots
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Assessor

Blinding implementation details:

Following lot consistency evaluation, data of subjects that received the individual vaccine lots were pooled for safety evaluation compared to the control group.

Arms

Are arms mutually exclusive?	No
Arm title	Combined Lot A, B, and C

Arm description:

V419 (Combined Lots A, B, and C) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; Pentacel™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age. Following lot consistency evaluation, data of subjects that received the individual vaccine lots were pooled for safety evaluation compared to the control group.

Arm type	Experimental
Investigational medicinal product name	PR5I
Investigational medicinal product code	V419
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, and 6 months of age.

Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral, 1 dose each at 2, 4, and 6 months of age.

Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection at 15 months of age.

Arm title	Control

Arm description:

PENTACEL™ 0.5 mL IM at 2, 4, 6, and 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age; and RECOMBIVAX HB™ 0.5 mL IM at 2 and 6 months of age.

Arm type	Active comparator
Investigational medicinal product name	PENTACEL™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Investigational medicinal product name	RECOMBIVAX HB™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2 and 6 months of age.

Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, 1 injection each at 2, 4, 6, and 15 months of age.

Investigational medicinal product name	RotaTeq™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral, 1 dose each at 2, 4, and 6 months of age.

Number of subjects in period 4	Combined Lot A, B, and C	Control
Started	2406	402
Completed	1974	370
Not completed	432	32
Physician decision	8	-

Consent withdrawn by subject	168	15
Technical problems	17	-
Adverse event, non-fatal	7	-
Death	4	-
Randomized but not vaccinated	-	1
Not specified	2	-
Lost to follow-up	203	13
Protocol deviation	23	3

Baseline characteristics

Reporting groups	
Reporting group title	V419 Lot A
Reporting group description:	
V419 (Lot A) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Reporting group title	V419 Lot B
Reporting group description:	
V419 (Lot B) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Reporting group title	V419 Lot C
Reporting group description:	
V419 (Lot C) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Reporting group title	Control
Reporting group description:	
PENTACEL™ 0.5 mL IM at 2, 4, 6, and 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age; and RECOMBIVAX HB™ 0.5 mL IM at 2 and 6 months of age.	

Reporting group values	V419 Lot A	V419 Lot B	V419 Lot C
Number of subjects	800	797	809
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	800	797	809
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: days			
arithmetic mean	64.6	64.4	64.7
standard deviation	± 6.7	± 6.2	± 6.6
Gender categorical Units: Subjects			
Female	377	366	380
Male	423	431	429

Reporting group values	Control	Total	
Number of subjects	402	2808	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	402	2808	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: days			
arithmetic mean	64.3		
standard deviation	± 6.6	-	
Gender categorical Units: Subjects			
Female	215	1338	
Male	187	1470	

End points

End points reporting groups

Reporting group title	V419 Lot A
Reporting group description:	
V419 (Lot A) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Reporting group title	V419 Lot B
Reporting group description:	
V419 (Lot B) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Reporting group title	V419 Lot C
Reporting group description:	
V419 (Lot C) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Reporting group title	Control
Reporting group description:	
PENTACEL™ 0.5 mL IM at 2, 4, 6, and 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age; and RECOMBIVAX HB™ 0.5 mL IM at 2 and 6 months of age.	
Reporting group title	V419 Lot A
Reporting group description:	
V419 (Lot A) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Reporting group title	V419 Lot B
Reporting group description:	
V419 (Lot B) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Reporting group title	V419 Lot C
Reporting group description:	
V419 (Lot C) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Reporting group title	Control
Reporting group description:	
PENTACEL™ 0.5 mL IM at 2, 4, 6, and 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age; and RECOMBIVAX HB™ 0.5 mL IM at 2 and 6 months of age.	
Reporting group title	V419 Lot A
Reporting group description:	
V419 (Lot A) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Reporting group title	V419 Lot B
Reporting group description:	
V419 (Lot B) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.	
Reporting group title	V419 Lot C
Reporting group description:	
V419 (Lot C) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; PENTACEL™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose	

at 2, 4, and 6 months of age.

Reporting group title	Control

Reporting group description:

PENTACEL™ 0.5 mL IM at 2, 4, 6, and 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age; and RECOMBIVAX HB™ 0.5 mL IM at 2 and 6 months of age.

Reporting group title	Combined Lot A, B, and C

Reporting group description:

V419 (Combined Lots A, B, and C) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; Pentacel™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age. Following lot consistency evaluation, data of subjects that received the individual vaccine lots were pooled for safety evaluation compared to the control group.

Reporting group title	Control

Reporting group description:

PENTACEL™ 0.5 mL IM at 2, 4, 6, and 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age; and RECOMBIVAX HB™ 0.5 mL IM at 2 and 6 months of age.

Primary: Geometric Mean Concentrations (GMC) for Antibodies to Polyribosylribitol Phosphate (PRP) Antigen

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Polyribosylribitol Phosphate (PRP) Antigen

End point description:

Subject serum samples were collected for testing with a radioimmunoassay for antibodies to Haemophilus influenza type b capsular polysaccharide polyribosylribitol phosphate (PRP). The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Primary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	604	596	595	288
Units: µg/mL				
geometric mean (confidence interval 95%)				
GMC for antibodies to PRP	5.51 (4.88 to 6.21)	6.1 (5.38 to 6.92)	6.59 (5.8 to 7.47)	3.76 (3.11 to 4.55)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1795			
Units: µg/mL				
geometric mean (confidence interval 95%)				

GMC for antibodies to PRP	6.05 (5.63 to 6.5)			

Statistical analyses

Statistical analysis title	Lot A/Lot B Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot A/Lot B ratio.	
Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1200
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot B)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.08

Notes:

[1] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot A/Lot C Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot A/Lot C ratio.	
Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1199
Analysis specification	Pre-specified
Analysis type	equivalence[2]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot C)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.02

Notes:

[2] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot B/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot B/Lot C ratio.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1191
Analysis specification	Pre-specified
Analysis type	equivalence[3]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot B/Lot C)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.12

Notes:

[3] - The estimates for GMC ratio is based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Combined Lots A, B, and C/Control Ratio

Statistical analysis description:

GMC ratio (Combined Lots A, B, and C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2083
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC ratio (Combined/Control)
Point estimate	1.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	1.98

Notes:

[4] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Primary: Geometric Mean Concentrations (GMC) for Antibodies to Hepatitis B Surface Antigen

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Hepatitis B Surface Antigen

End point description:

Subject serum samples were collected for testing with an enhanced chemiluminescence assay for antibodies to Hepatitis B Surface Antigen. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Primary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	588	599	580	286
Units: mIU/mL				
geometric mean (confidence interval 95%)				
GMC for antibodies to Hepatitis B Surface Antigen	1195.96 (1081.62 to 1322.39)	1376.86 (1264.74 to 1498.92)	1414.52 (1297.52 to 1542.06)	609.08 (515.29 to 719.93)

Statistical analyses

Statistical analysis title	Lot A/Lot B Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot A/Lot B ratio.	
Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1187
Analysis specification	Pre-specified
Analysis type	equivalence[5]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot B)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	0.98

Notes:

[5] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot A/Lot C Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot A/Lot C ratio.	
Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1168
Analysis specification	Pre-specified
Analysis type	equivalence[6]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot C)
Point estimate	0.85

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	0.96

Notes:

[6] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot B/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot B/Lot C ratio.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	equivalence[7]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot B/Lot C)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.11

Notes:

[7] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Primary: Geometric Mean Concentrations (GMC) for Antibodies to Diphtheria Toxin

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Diphtheria Toxin

End point description:

Subject serum samples were collected for testing with a micrometabolic inhibition test for neutralizing antibodies to diphtheria toxin. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Primary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	622	625	618	301
Units: IU/mL				
geometric mean (confidence interval 95%)				

GMC for Antibodies to Diphtheria Toxin	0.37 (0.34 to 0.4)	0.36 (0.33 to 0.4)	0.38 (0.34 to 0.41)	0.4 (0.35 to 0.45)

Statistical analyses

Statistical analysis title	Lot A/Lot B Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot A/Lot B ratio.	
Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1247
Analysis specification	Pre-specified
Analysis type	equivalence[8]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot B)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.07

Notes:

[8] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot A/Lot C Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot A/Lot C ratio.	
Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1240
Analysis specification	Pre-specified
Analysis type	equivalence[9]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot C)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.09

Notes:

[9] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot B/Lot C Ratio

Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot B/Lot C ratio.	
Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1243
Analysis specification	Pre-specified
Analysis type	equivalence[10]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot B/Lot C)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.14

Notes:

[10] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Primary: Geometric Mean Concentrations (GMC) for Antibodies to Tetanus Toxin

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Tetanus Toxin

End point description:

Subject serum samples were collected for testing with an enzyme-linked immunosorbent assay (ELISA) for anti-tetanus antibodies. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Primary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	622	609	612	300
Units: IU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Tetanus Toxin	1.59 (1.51 to 1.67)	1.63 (1.55 to 1.71)	1.55 (1.48 to 1.63)	0.89 (0.81 to 0.97)

Statistical analyses

Statistical analysis title	Lot A/Lot B Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot A/Lot B ratio.	
Comparison groups	V419 Lot A v V419 Lot B

Number of subjects included in analysis	1231
Analysis specification	Pre-specified
Analysis type	equivalence[11]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot B)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.04

Notes:

[11] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot A/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot A/Lot C ratio.

Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1234
Analysis specification	Pre-specified
Analysis type	equivalence[12]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot C)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.09

Notes:

[12] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot B/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot B/Lot C ratio.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1221
Analysis specification	Pre-specified
Analysis type	equivalence[13]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot B/Lot C)
Point estimate	1.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.13

Notes:

[13] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Primary: Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Toxin

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Toxin

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis toxin. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Primary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	647	634	622	309
Units: EU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Pertussis Toxin	100.83 (95.98 to 105.91)	96.82 (92.1 to 101.79)	98.52 (93.84 to 103.43)	82.45 (77.26 to 87.98)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1903			
Units: EU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Pertussis Toxin	98.72 (95.96 to 101.57)			

Statistical analyses

Statistical analysis title	Lot A/Lot B Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot A/Lot B ratio.

Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1281
Analysis specification	Pre-specified
Analysis type	equivalence[14]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot B)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.1

Notes:

[14] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot A/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot A/Lot C ratio.

Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1269
Analysis specification	Pre-specified
Analysis type	equivalence[15]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot C)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.09

Notes:

[15] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot B/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot B/Lot C ratio.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1256
Analysis specification	Pre-specified
Analysis type	equivalence[16]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot B/Lot C)
Point estimate	0.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.06

Notes:

[16] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Combined Lots A, B, and C/Control Ratio

Statistical analysis description:

GMC ratio (Combined Lots A, B, and C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2212
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC ratio (Combined Lots/Control)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	1.29

Notes:

[17] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio ≥0.67.

Primary: Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Filamentous Hemagglutinin (FHA)

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Filamentous Hemagglutinin (FHA)

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis FHA. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Primary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	644	631	628	312
Units: EU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Pertussis FHA	43.98 (41.45 to 46.66)	49.19 (46.52 to 52.02)	56.93 (53.73 to 60.31)	73.25 (67.94 to 78.97)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1903			
Units: EU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Pertussis FHA	49.7 (48.06 to 51.4)			

Statistical analyses

Statistical analysis title	Lot A/Lot B Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot A/Lot B ratio.	
Comparison groups	V419 Lot B v V419 Lot A
Number of subjects included in analysis	1275
Analysis specification	Pre-specified
Analysis type	equivalence[18]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot B)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	0.96

Notes:

[18] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot A/Lot C Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot A/Lot C ratio.	
Comparison groups	V419 Lot A v V419 Lot C

Number of subjects included in analysis	1272
Analysis specification	Pre-specified
Analysis type	equivalence[19]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot C)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.83

Notes:

[19] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot B/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot B/Lot C ratio.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1259
Analysis specification	Pre-specified
Analysis type	equivalence[20]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot B/Lot C)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	0.94

Notes:

[20] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Combined Lots A, B, and C/Control Ratio

Statistical analysis description:

GMC ratio (Combined Lots A, B, and C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2215
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
P-value	= 0.419
Method	ANCOVA
Parameter estimate	GMC ratio (Combined Lots/Control)
Point estimate	0.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.73

Notes:

[21] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Primary: Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Pertactin

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Pertactin

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis pertactin. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Primary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	632	616	611	303
Units: EU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Pertussis Pertactin	51.3 (47.46 to 55.44)	52.32 (47.85 to 57.21)	54.78 (50.33 to 59.61)	50.96 (45.38 to 57.21)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1859			
Units: EU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Pertussis Pertactin	52.76 (50.27 to 55.37)			

Statistical analyses

Statistical analysis title	Lot A/Lot B Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot A/Lot B ratio.

Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1248
Analysis specification	Pre-specified
Analysis type	equivalence[22]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot B)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.09

Notes:

[22] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot A/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot A/Lot C ratio.

Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1243
Analysis specification	Pre-specified
Analysis type	equivalence[23]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot C)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.05

Notes:

[23] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot B/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot B/Lot C ratio.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1227
Analysis specification	Pre-specified
Analysis type	equivalence[24]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot B/Lot C)
Point estimate	0.96

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.08

Notes:

[24] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Combined Lots A, B, and C/Control Ratio

Statistical analysis description:

GMC ratio (Combined Lots A, B, and C/Control)

Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2162
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC ratio (Combined Lots/Control)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.17

Notes:

[25] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Primary: Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Fimbriae

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Fimbriae

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis fimbriae. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Primary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	641	632	623	309
Units: EU/mL				
geometric mean (confidence interval 95%)				

GMC for Antibodies to Pertussis Fimbriae	228.78 (213.87 to 244.73)	286.74 (268.86 to 305.81)	283.28 (264.52 to 303.36)	175.65 (159.14 to 193.87)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1896			
Units: EU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Pertussis Fimbriae	264.61 (254.54 to 275.07)			

Statistical analyses

Statistical analysis title	Lot A/Lot B Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot A/Lot B ratio.	
Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1273
Analysis specification	Pre-specified
Analysis type	equivalence[26]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot B)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.85

Notes:

[26] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot A/Lot C Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMC of Lot A/Lot C ratio.	
Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1264
Analysis specification	Pre-specified
Analysis type	equivalence[27]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot A/Lot C)
Point estimate	0.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	0.87

Notes:

[27] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot B/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMC of Lot B/Lot C ratio.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1255
Analysis specification	Pre-specified
Analysis type	equivalence[28]
Method	ANCOVA
Parameter estimate	GMC ratio (Lot B/Lot C)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.11

Notes:

[28] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMC ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Combined Lots A, B, and C/Control Ratio

Statistical analysis description:

GMC ratio (Combined Lots A, B, and C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2205
Analysis specification	Pre-specified
Analysis type	non-inferiority[29]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC ratio (Combined Lots/Control)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.37
upper limit	1.66

Notes:

[29] - The estimates for GMC ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Primary: Geometric Mean Titer (GMT) for Antibodies to Poliovirus Type 1

End point title	Geometric Mean Titer (GMT) for Antibodies to Poliovirus Type 1

End point description:

Subject serum samples were collected for testing with a micrometabolic inhibition test for neutralizing antibodies to poliovirus type 1. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Primary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	630	632	628	307
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
GMT for Antibodies to Poliovirus Type 1	579.77 (533.82 to 629.68)	684.68 (628.4 to 746.01)	666.18 (612.3 to 724.79)	269.95 (232.21 to 313.83)

Statistical analyses

Statistical analysis title	Lot A/Lot B Ratio

Statistical analysis description:

Lot consistency analysis regarding GMT of Lot A/Lot B ratio.

Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1262
Analysis specification	Pre-specified
Analysis type	equivalence[30]
Method	ANCOVA
Parameter estimate	GMT ratio (Lot A/Lot B)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	0.96

Notes:

[30] - The estimates for GMT ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMT ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot A/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMT of Lot A/Lot C ratio.

Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1258
Analysis specification	Pre-specified
Analysis type	equivalence[31]
Method	ANCOVA
Parameter estimate	GMT ratio (Lot A/Lot C)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	0.99

Notes:

[31] - The estimates for GMT ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMT ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot B/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMT of Lot B/Lot C ratio.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1260
Analysis specification	Pre-specified
Analysis type	equivalence[32]
Method	ANCOVA
Parameter estimate	GMT ratio (Lot B/Lot C)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.15

Notes:

[32] - The estimates for GMT ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMT ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Primary: Geometric Mean Titer (GMT) for Antibodies to Poliovirus Type 2

End point title	Geometric Mean Titer (GMT) for Antibodies to Poliovirus Type 2

End point description:

Subject serum samples were collected for testing with a micrometabolic inhibition test for neutralizing antibodies to Poliovirus Type 2. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Primary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	630	632	633	307
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
GMT to Antibodies to Poliovirus Type 2	1212.4 (1116.4 to 1316.65)	1276.56 (1172.86 to 1389.43)	1359.78 (1248.13 to 1481.42)	846.14 (751.81 to 952.3)

Statistical analyses

Statistical analysis title	Lot A/Lot B Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMT of Lot A/Lot B ratio.	
Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1262
Analysis specification	Pre-specified
Analysis type	equivalence[33]
Method	ANCOVA
Parameter estimate	GMT ratio (Lot A/Lot B)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.05

Notes:

[33] - The estimates for GMT ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMT ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot B/Lot C Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMT of Lot B/Lot C ratio.	
Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1265
Analysis specification	Pre-specified
Analysis type	equivalence[34]
Method	ANCOVA
Parameter estimate	GMT ratio (Lot B/Lot C)
Point estimate	0.98

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.09

Notes:

[34] - The estimates for GMT ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMT ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot A/Lot C Ratio

Statistical analysis description:

Lot consistency analysis regarding GMT of Lot A/Lot C ratio.

Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	equivalence[35]
Method	ANCOVA
Parameter estimate	GMT ratio (Lot A/Lot C)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.02

Notes:

[35] - The estimates for GMT ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMT ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Primary: Geometric Mean Titer (GMT) for Antibodies to Poliovirus Type 3

End point title	Geometric Mean Titer (GMT) for Antibodies to Poliovirus Type 3

End point description:

Subject serum samples were collected for testing with a micrometabolic inhibition test for neutralizing antibodies Poliovirus Type 3. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Primary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	624	625	625	304
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				

GMT for Antibodies to Poliovirus Type 3	901.7 (819.52 to 992.12)	851.34 (772.96 to 937.66)	825.31 (746.52 to 912.42)	784.24 (682.28 to 901.44)

Statistical analyses

Statistical analysis title	Lot A/Lot B Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMT of Lot A/Lot B ratio.	
Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1249
Analysis specification	Pre-specified
Analysis type	equivalence[36]
Method	ANCOVA
Parameter estimate	GMT ratio (Lot A/Lot B)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.22

Notes:

[36] - The estimates for GMT ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMT ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot B/Lot C Ratio
Statistical analysis description:	
Lot consistency analysis regarding GMT of Lot B/Lot C ratio.	
Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1250
Analysis specification	Pre-specified
Analysis type	equivalence[37]
Method	ANCOVA
Parameter estimate	GMT ratio (Lot B/Lot C)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.19

Notes:

[37] - The estimates for GMT ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMT ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Statistical analysis title	Lot A/Lot C Ratio

Statistical analysis description:	
Lot consistency analysis regarding GMT of Lot A/Lot C ratio.	
Comparison groups	V419 Lot C v V419 Lot A
Number of subjects included in analysis	1249
Analysis specification	Pre-specified
Analysis type	equivalence[38]
Method	ANCOVA
Parameter estimate	GMT ratio (Lot A/Lot C)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.26

Notes:

[38] - The estimates for GMT ratio are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the GMT ratios between any 2 lots were within the equivalence margin (0.67 to 1.5).

Secondary: Percentage of Subjects Responding to Polyribosylribitol Phosphate (PRP) Antigen

End point title	Percentage of Subjects Responding to Polyribosylribitol Phosphate (PRP) Antigen

End point description:

Subject serum samples were collected for testing with a radioimmunoassay for antibodies to Haemophilus influenza type b capsular polysaccharide polyribosylribitol phosphate (PRP). Sera response or endpoint was defined as a titer ≥0.15 µg/mL and ≥1.0 µg/mL. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Secondary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	604	596	596	288
Units: Percentage of subjects				
number (confidence interval 95%)				
PRP titer ≥1 µg/mL	86.75 (83.79 to 89.36)	87.25 (84.3 to 89.82)	88.4 (85.55 to 90.86)	79.51 (74.39 to 84.02)
PRP titer ≥0.15 µg/mL	99.01 (97.85 to 99.63)	98.32 (96.94 to 99.19)	97.82 (96.29 to 98.83)	96.18 (93.27 to 98.08)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1795			

Units: Percentage of subjects				
number (confidence interval 95%)				
PRP titer ≥1 µg/mL	87.47 (85.84 to 88.96)			
PRP titer ≥0.15 µg/mL	98.38 (97.69 to 98.92)			

Statistical analyses

Statistical analysis title	Lot A-Lot B Difference ≥1 ug/mL
Statistical analysis description:	
Response rate analysis of Lot A-Lot B mean difference.	
Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1200
Analysis specification	Pre-specified
Analysis type	equivalence[39]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.31
upper limit	3.35

Notes:

[39] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot A-Lot C Difference ≥1 ug/mL
Statistical analysis description:	
Response rate analysis of Lot A-Lot C mean difference.	
Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1200
Analysis specification	Pre-specified
Analysis type	equivalence[40]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.38
upper limit	2.12

Notes:

[40] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot B-Lot C Difference ≥1 ug/mL
Statistical analysis description:	
Response rate analysis of Lot B-Lot C mean difference.	

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1192
Analysis specification	Pre-specified
Analysis type	equivalence[41]
Parameter estimate	Mean difference (final values)
Point estimate	-1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.89
upper limit	2.58

Notes:

[41] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Combined Lots A, B, C-Control Difference ≥1 ug/mL

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2083
Analysis specification	Pre-specified
Analysis type	non-inferiority[42]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	7.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.38
upper limit	13.17

Notes:

[42] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-10%.

Statistical analysis title	Combined Lots-Control Difference ≥ 0.15 ug/mL

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2083
Analysis specification	Pre-specified
Analysis type	non-inferiority[43]
P-value	< 0.001 [44]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	5.12

Notes:

[43] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-5%.

[44] - One-sided p-value

Secondary: Percentage of Subjects Responding to Hepatitis B Surface Antigen

End point title	Percentage of Subjects Responding to Hepatitis B Surface Antigen

End point description:

Subject serum samples were collected for testing with an enhanced chemiluminescence assay for antibodies to Hepatitis B Surface Antigen. Sera response or endpoint was defined as a titer ≥ 10 mIU/mL. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Secondary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	588	599	580	286
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Hepatitis B	99.66 (98.78 to 99.96)	100 (99.39 to 100)	100 (99.37 to 100)	98.95 (96.97 to 99.78)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1767			
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Hepatitis B	99.89 (99.59 to 99.99)			

Statistical analyses

Statistical analysis title	Lot A-Lot B Difference

Statistical analysis description:

Response rate analysis of Lot A-Lot B mean difference.

Comparison groups	V419 Lot A v V419 Lot B

Number of subjects included in analysis	1187
Analysis specification	Pre-specified
Analysis type	equivalence[45]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	0.3

Notes:

[45] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot A-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot A-Lot C mean difference.

Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1168
Analysis specification	Pre-specified
Analysis type	equivalence[46]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	0.32

Notes:

[46] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot B-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot B-Lot C mean difference.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	equivalence[47]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.64
upper limit	0.66

Notes:

[47] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Combined Lots A, B, C-Control Difference
Statistical analysis description:	
Response rate analysis of Combined Lots A, B, and C-Control mean difference.	
Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2053
Analysis specification	Pre-specified
Analysis type	non-inferiority[48]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	2.9

Notes:

[48] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-10%.

Secondary: Percentage of Subjects Responding to Diphtheria Toxin

End point title	Percentage of Subjects Responding to Diphtheria Toxin
End point description:	
Subject serum samples were collected for testing with a micrometabolic inhibition test for neutralizing antibodies to diphtheria toxin. Sera response or endpoint was defined as a titer ≥ 0.1 IU/mL. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.	
End point type	Secondary
End point timeframe:	
Postdose 3 (Month 7)	

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	622	625	618	301
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Diphtheria	85.05 (82 to 87.76)	84.8 (81.74 to 87.52)	86.41 (83.45 to 89.01)	87.71 (83.46 to 91.2)

End point values	Combined Lot A, B, and C			

Subject group type	Reporting group			
Number of subjects analysed	1865			
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Diphtheria	85.42 (83.73 to 86.99)			

Statistical analyses

Statistical analysis title	Lot A-Lot B Difference
Statistical analysis description:	
Response rate analysis of Lot A-Lot B mean difference.	
Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1247
Analysis specification	Pre-specified
Analysis type	equivalence[49]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.74
upper limit	4.24

Notes:

[49] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot B-Lot C Difference
Statistical analysis description:	
Response rate analysis of Lot B-Lot C mean difference.	
Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1243
Analysis specification	Pre-specified
Analysis type	equivalence[50]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.56
upper limit	2.28

Notes:

[50] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot A-Lot C Difference

Statistical analysis description:	
Response rate analysis of Lot A-Lot C mean difference.	
Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1240
Analysis specification	Pre-specified
Analysis type	equivalence[51]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.26
upper limit	2.57

Notes:

[51] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Combined Lots A, B, C-Control Difference
Statistical analysis description:	
Response rate analysis of Combined Lots A, B, and C-Control mean difference.	
Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2166
Analysis specification	Pre-specified
Analysis type	non-inferiority[52]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-2.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.02
upper limit	2.09

Notes:

[52] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-10%.

Secondary: Percentage of Subjects Responding to Tetanus Toxin

End point title	Percentage of Subjects Responding to Tetanus Toxin

End point description:

Subject serum samples were collected for testing with an ELISA for anti-tetanus antibodies. Sera response or endpoint was defined as a titer ≥ 0.1 IU/mL. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Secondary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	622	609	612	300
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Tetanus Toxin	99.84 (99.11 to 100)	100 (99.4 to 100)	100 (99.4 to 100)	98.67 (96.62 to 99.64)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1843			
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Tetanus Toxin	99.95 (99.7 to 100)			

Statistical analyses

Statistical analysis title	Lot A-Lot B Difference
Statistical analysis description:	
Response rate analysis of Lot A-Lot B mean difference.	
Comparison groups	V419 Lot B v V419 Lot A
Number of subjects included in analysis	1231
Analysis specification	Pre-specified
Analysis type	equivalence[53]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	0.47

Notes:

[53] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Lot A-Lot C Difference
Statistical analysis description:	
Response rate analysis of Lot A-Lot C mean difference.	
Comparison groups	V419 Lot A v V419 Lot C

Number of subjects included in analysis	1234
Analysis specification	Pre-specified
Analysis type	equivalence[54]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.47

Notes:

[54] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Lot B-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot B-Lot C mean difference.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1221
Analysis specification	Pre-specified
Analysis type	equivalence[55]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.63
upper limit	0.62

Notes:

[55] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Combined Lots A, B, C-Control Difference

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2143
Analysis specification	Pre-specified
Analysis type	non-inferiority[56]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	3.33

Notes:

[56] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-5%.

Secondary: Percentage of Subjects Responding to Pertussis Toxin

End point title	Percentage of Subjects Responding to Pertussis Toxin

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis toxin. Sera response or endpoint was defined as follows: (1) if the pre dose titer was <4 times the lower limit of quantitation (4X LLOQ) then the post dose titer was ≥4X LLOQ; (2) if the predose titer was ≥4X LLOQ then the post dose titer was ≥ the predose titer. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Secondary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	596	585	580	289
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Pertussis	99.33 (98.29 to 99.82)	97.61 (96.02 to 98.69)	98.97 (97.76 to 99.62)	97.92 (95.54 to 99.23)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1761			
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Pertussis	98.64 (97.98 to 99.12)			

Statistical analyses

Statistical analysis title	Lot A-Lot B Difference

Statistical analysis description:

Response rate analysis of Lot A-Lot B mean difference.

Comparison groups	V419 Lot A v V419 Lot B

Number of subjects included in analysis	1181
Analysis specification	Pre-specified
Analysis type	equivalence[57]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	3.4

Notes:

[57] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot A-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot A-Lot C mean difference.

Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1176
Analysis specification	Pre-specified
Analysis type	equivalence[58]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.77
upper limit	1.63

Notes:

[58] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot B-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot B-Lot C mean difference.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1165
Analysis specification	Pre-specified
Analysis type	equivalence[59]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.03
upper limit	0.15

Notes:

[59] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Combined Lots A, B, C-Control Difference

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2050
Analysis specification	Pre-specified
Analysis type	non-inferiority[60]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	3.14

Notes:

[60] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-10%.

Secondary: Percentage of Subjects Responding to Pertussis Filamentous Hemagglutinin (FHA)

End point title	Percentage of Subjects Responding to Pertussis Filamentous Hemagglutinin (FHA)

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis filamentous hemagglutinin. Sera response or endpoint was defined as follows: (1) if the pre dose titer was <4X LLOQ then the post dose titer was ≥4X LLOQ; (2) if the predose titer was ≥4X LLOQ then the post dose titer was ≥ the predose titer. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Secondary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	620	615	601	304
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Pertussis FHA	85.97 (82.98 to 88.61)	87.32 (84.43 to 89.84)	89.02 (86.24 to 91.4)	92.11 (88.48 to 94.88)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1836			
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Pertussis FHA	87.42 (85.81 to 88.9)			

Statistical analyses

Statistical analysis title	Lot A-Lot B Difference
Statistical analysis description:	
Response rate analysis of Lot A-Lot B mean difference.	
Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1235
Analysis specification	Pre-specified
Analysis type	equivalence[61]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.17
upper limit	2.47

Notes:

[61] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot A-Lot C Difference
Statistical analysis description:	
Response rate analysis of Lot A-Lot C mean difference.	
Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1221
Analysis specification	Pre-specified
Analysis type	equivalence[62]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-3.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.79
upper limit	0.67

Notes:

[62] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot B-Lot C Difference

Statistical analysis description:	
Response rate analysis of Lot B-Lot C mean difference.	
Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1216
Analysis specification	Pre-specified
Analysis type	equivalence[63]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.37
upper limit	1.94

Notes:

[63] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Combined Lots A, B, C-Control Difference
Statistical analysis description:	
Response rate analysis of Combined Lots A, B, C-Control mean difference.	
Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2140
Analysis specification	Pre-specified
Analysis type	non-inferiority[64]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.73
upper limit	-0.86

Notes:

[64] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-10%.

Secondary: Percentage of Subjects Responding to Pertussis Pertactin (PRN)

End point title	Percentage of Subjects Responding to Pertussis Pertactin (PRN)

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis pertactin (PRN). Sera response or endpoint was defined as follows: (1) if the pre dose titer was <4X LLOQ then the postdose titer was ≥4X LLOQ; (2) if the predose titer was ≥4X LLOQ then the postdose titer was ≥ the predose titer. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Secondary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	590	574	560	286
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Pertussis PRN	81.19 (77.79 to 84.26)	78.4 (74.8 to 81.7)	78.75 (75.13 to 82.07)	76.22 (70.86 to 81.04)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1724			
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Pertussis PRN	79.47 (77.48 to 81.35)			

Statistical analyses

Statistical analysis title	Lot A-Lot B Difference
Statistical analysis description:	
Response rate analysis of Lot A-Lot B mean difference.	
Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1164
Analysis specification	Pre-specified
Analysis type	equivalence[65]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	2.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.83
upper limit	7.39

Notes:

[65] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot A-Lot C Difference
Statistical analysis description:	
Response rate analysis of Lot A-Lot C mean difference.	
Comparison groups	V419 Lot A v V419 Lot C

Number of subjects included in analysis	1150
Analysis specification	Pre-specified
Analysis type	equivalence[66]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	2.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.21
upper limit	7.06

Notes:

[66] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot B-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot B-Lot C mean difference.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1134
Analysis specification	Pre-specified
Analysis type	equivalence[67]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.14
upper limit	4.42

Notes:

[67] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Combined Lots A, B, C-Control Difference

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2010
Analysis specification	Pre-specified
Analysis type	non-inferiority[68]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	3.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	8.85

Notes:

[68] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-10%.

Secondary: Percentage of Subjects Responding to Pertussis Fimbriae

End point title	Percentage of Subjects Responding to Pertussis Fimbriae

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis fimbriae. Sera response or endpoint was defined as follows: (1) if the pre dose titer was <4X LLOQ then the post dose titer was ≥4X LLOQ; (2) if the predose titer was ≥4X LLOQ then the post dose titer was ≥ the predose titer. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Secondary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	613	611	594	298
Units: Percentage of subjects				
number (confidence interval 95%)				
Subjects Responding to Pertussis Fimbriae	86.95 (84.02 to 89.51)	91 (88.44 to 93.15)	91.08 (88.49 to 93.25)	86.91 (82.55 to 90.53)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1818			
Units: Percentage of subjects				
number (confidence interval 95%)				
Subjects Responding to Pertussis Fimbriae	89.66 (88.17 to 91.02)			

Statistical analyses

Statistical analysis title	Lot A-Lot B Difference

Statistical analysis description:

Response rate analysis of Lot A-Lot B mean difference.

Comparison groups	V419 Lot A v V419 Lot B

Number of subjects included in analysis	1224
Analysis specification	Pre-specified
Analysis type	equivalence[69]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-4.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.69
upper limit	-0.63

Notes:

[69] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot A-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot A-Lot C mean difference.

Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1207
Analysis specification	Pre-specified
Analysis type	equivalence[70]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-4.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.75
upper limit	-0.66

Notes:

[70] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Lot B-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot B-Lot C mean difference.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1205
Analysis specification	Pre-specified
Analysis type	equivalence[71]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.32
upper limit	3.2

Notes:

[71] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-10% to 10%).

Statistical analysis title	Combined Lots A, B, C-Control Difference

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2116
Analysis specification	Pre-specified
Analysis type	non-inferiority[72]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	2.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	7.36

Notes:

[72] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-10%.

Secondary: Percentage of Subjects Responding to Poliovirus Type 1

End point title	Percentage of Subjects Responding to Poliovirus Type 1

End point description:

Subject serum samples were collected for testing with a microneutralization inhibition test for neutralizing antibodies to Poliovirus Type 1. Sera response or endpoint is defined as a titer ≥8. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Secondary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	630	632	628	307
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Poliovirus 1	100 (99.42 to 100)	100 (99.42 to 100)	100 (99.41 to 100)	99.35 (97.67 to 99.92)

End point values	Combined Lot A, B, and C			

Subject group type	Reporting group			
Number of subjects analysed	1890			
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Poliovirus 1	100 (99.81 to 100)			

Statistical analyses

Statistical analysis title	Lot A-Lot B Difference

Statistical analysis description:

Response rate analysis of Lot A-Lot B mean difference.

Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1262
Analysis specification	Pre-specified
Analysis type	equivalence[73]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.61

Notes:

[73] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Lot A-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot A-Lot C mean difference.

Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1258
Analysis specification	Pre-specified
Analysis type	equivalence[74]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.61

Notes:

[74] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Lot B-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot B-Lot C mean difference.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1260
Analysis specification	Pre-specified
Analysis type	equivalence[75]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.61

Notes:

[75] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Combined Lots A, B, C-Control Difference

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2197
Analysis specification	Pre-specified
Analysis type	non-inferiority[76]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	2.36

Notes:

[76] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-5%.

Secondary: Percentage of Subjects Responding to Poliovirus Type 2

End point title	Percentage of Subjects Responding to Poliovirus Type 2

End point description:

Subject serum samples were collected for testing with a microneutralization inhibition test for neutralizing antibodies to Poliovirus Type 2. Sera response or endpoint is defined as a titer ≥8. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Secondary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	630	632	633	307
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Poliovirus 2	100 (99.42 to 100)	100 (99.42 to 100)	100 (99.42 to 100)	100 (98.81 to 100)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1895			
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Poliovirus 2	100 (99.81 to 100)			

Statistical analyses

Statistical analysis title	Lot A-Lot B Difference
Statistical analysis description:	
Response rate analysis of Lot A-Lot B mean difference.	
Comparison groups	V419 Lot A v V419 Lot B
Number of subjects included in analysis	1262
Analysis specification	Pre-specified
Analysis type	equivalence[77]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.61

Notes:

[77] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Lot A-Lot C Difference
Statistical analysis description:	
Response rate analysis of Lot A-Lot C mean difference.	
Comparison groups	V419 Lot A v V419 Lot C

Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	equivalence[78]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.6

Notes:

[78] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Lot B-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot B-Lot C mean difference.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1265
Analysis specification	Pre-specified
Analysis type	equivalence[79]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.6

Notes:

[79] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Combined Lots A, B, C-Control Difference

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2202
Analysis specification	Pre-specified
Analysis type	non-inferiority[80]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	1.24

Notes:

[80] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-5%.

Secondary: Percentage of Subjects Responding to Poliovirus Type 3

End point title	Percentage of Subjects Responding to Poliovirus Type 3

End point description:

Subject serum samples were collected for testing with a microneutralization inhibition test for neutralizing antibodies to Poliovirus Type 3. Sera response or endpoint is defined as a titer ≥8. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Secondary

End point timeframe:

Postdose 3 (Month 7)

End point values	V419 Lot A	V419 Lot B	V419 Lot C	Control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	624	625	625	304
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Poliovirus 3	100 (99.41 to 100)	100 (99.41 to 100)	100 (99.41 to 100)	99.67 (98.18 to 99.99)

End point values	Combined Lot A, B, and C			
Subject group type	Reporting group			
Number of subjects analysed	1874			
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Poliovirus 3	100 (99.8 to 100)			

Statistical analyses

Statistical analysis title	Lot A-Lot B Difference

Statistical analysis description:

Response rate analysis of Lot A-Lot B mean difference.

Comparison groups	V419 Lot A v V419 Lot B

Number of subjects included in analysis	1249
Analysis specification	Pre-specified
Analysis type	equivalence[81]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.61

Notes:

[81] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Lot A-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot A-Lot C mean difference.

Comparison groups	V419 Lot A v V419 Lot C
Number of subjects included in analysis	1249
Analysis specification	Pre-specified
Analysis type	equivalence[82]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.61

Notes:

[82] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Lot B-Lot C Difference

Statistical analysis description:

Response rate analysis of Lot B-Lot C mean difference.

Comparison groups	V419 Lot B v V419 Lot C
Number of subjects included in analysis	1250
Analysis specification	Pre-specified
Analysis type	equivalence[83]
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.61

Notes:

[83] - Response rate differences were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Equivalence required that the lower and upper limits of the 95% confidence interval of the response rates between any 2 lots were within the equivalence margin (-5% to 5%).

Statistical analysis title	Combined Lots A, B, C-Control Difference

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2178
Analysis specification	Pre-specified
Analysis type	non-inferiority[84]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	1.85

Notes:

[84] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-5%.

Secondary: Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Toxin

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Toxin

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis toxin. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 4.

End point type	Secondary

End point timeframe:

Postdose 4 (Month 16)

End point values	Combined Lot A, B, and C	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1744	271		
Units: EU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Pertussis Toxin	110.61 (106.92 to 114.42)	102.82 (93.7 to 112.82)		

Statistical analyses

Statistical analysis title	Combined Lots A, B, and C/Control Ratio
Statistical analysis description:	
GMC ratio (Combined Lots A, B, and C/Control)	
Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2015
Analysis specification	Pre-specified
Analysis type	non-inferiority[85]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.17

Notes:

[85] - The estimates for GMC, GMC ratio, and p-value are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Secondary: Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Filamentous Hemagglutinin (FHA)

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Filamentous Hemagglutinin (FHA)

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis filamentous hemagglutinin. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 4.

End point type	Secondary

End point timeframe:

Postdose 4 (Month 16)

End point values	Combined Lot A, B, and C	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1742	271		
Units: EU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Pertussis FHA	106.3 (102.73 to 110)	121 (110.19 to 132.87)		

Statistical analyses

Statistical analysis title	Combined Lots A, B, and C/Control Ratio

Statistical analysis description:	
GMC ratio (Combined Lots A, B, and C/Control)	
Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2013
Analysis specification	Pre-specified
Analysis type	non-inferiority[86]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	0.95

Notes:

[86] - The estimates for GMC, GMC ratio, and p-value are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Secondary: Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Pertactin

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Pertactin

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis pertactin. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 4.

End point type	Secondary

End point timeframe:

Postdose 4 (Month 16)

End point values	Combined Lot A, B, and C	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1746	271		
Units: EU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Pertussis Pertactin	104.51 (100.14 to 109.07)	142.32 (126.68 to 159.89)		

Statistical analyses

Statistical analysis title	Combined Lots A, B, and C/Control Ratio

Statistical analysis description:	
GMC ratio (Combined Lots A, B, and C/Control)	
Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2017
Analysis specification	Pre-specified
Analysis type	non-inferiority[87]
P-value	= 0.035
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.83

Notes:

[87] - The estimates for GMC, GMC ratio, and p-value are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Secondary: Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Fimbriae

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Pertussis Fimbriae

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis fimbriae. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 4.

End point type	Secondary

End point timeframe:

Postdose 4 (Month 16)

End point values	Combined Lot A, B, and C	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1746	271		
Units: EU/mL				
geometric mean (confidence interval 95%)				
GMC for Antibodies to Pertussis Fimbriae	451.04 (433.21 to 469.6)	337.79 (299.43 to 381.05)		

Statistical analyses

Statistical analysis title	Combined Lots A, B, and C/Control Ratio

Statistical analysis description:	
GMC ratio (Combined Lots A, B, and C/Control)	
Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2017
Analysis specification	Pre-specified
Analysis type	non-inferiority[88]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	1.46

Notes:

[88] - The estimates for GMC, GMC ratio, and p-value are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Secondary: Percentage of Subjects Responding to Pertussis Toxin

End point title	Percentage of Subjects Responding to Pertussis Toxin

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis toxin. Sera response or endpoint was defined as follows: 1) if the predose titer was <4X LLOQ then the postdose titer was ≥4X LLOQ; 2) if the predose titer was ≥4X LLOQ then the postdose titer was ≥ the predose titer. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 4.

End point type	Secondary

End point timeframe:

Postdose 4 (Month 16)

End point values	Combined Lot A, B, and C	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1616	254		
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Pertussis	98.51 (97.8 to 99.05)	98.43 (96.02 to 99.57)		

Statistical analyses

Statistical analysis title	Combined Lots A, B, C-Control Difference
Statistical analysis description:	
Response rate analysis of Combined Lots A, B, and C-Control mean difference.	
Comparison groups	Combined Lot A, B, and C v Control

Number of subjects included in analysis	1870
Analysis specification	Pre-specified
Analysis type	non-inferiority[89]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.11
upper limit	2.58

Notes:

[89] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-10%.

Secondary: Percentage of Subjects Responding to Pertussis Filamentous Hemagglutinin (FHA)

End point title	Percentage of Subjects Responding to Pertussis Filamentous Hemagglutinin (FHA)

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis filamentous hemagglutinin. Sera response or endpoint was defined as follows: (1) if the predose titer was <4X LLOQ then the postdose titer was ≥4X LLOQ; (2) if the predose titer was ≥4X LLOQ then the post dose titer was ≥ the predose titer. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 4.

End point type	Secondary

End point timeframe:

Postdose 4 (Month 16)

End point values	Combined Lot A, B, and C	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1669	261		
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Pertussis FHA	95.33 (94.2 to 96.29)	95.4 (92.11 to 97.6)		

Statistical analyses

Statistical analysis title	Combined Lots A, B, C-Control Difference

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Combined Lot A, B, and C v Control

Number of subjects included in analysis	1930
Analysis specification	Pre-specified
Analysis type	non-inferiority[90]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.41
upper limit	3.22

Notes:

[90] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-10%.

Secondary: Percentage of Subjects Responding to Pertussis Pertactin (PRN)

End point title	Percentage of Subjects Responding to Pertussis Pertactin (PRN)

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis pertactin. Sera response or endpoint was defined as follows: (1) if the predose titer was <4X LLOQ then the postdose titer was ≥4X LLOQ; (2) if the predose titer was ≥4X LLOQ then the postdose titer was ≥ the predose titer. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 4.

End point type	Secondary

End point timeframe:

Postdose 4 (Month 16)

End point values	Combined Lot A, B, and C	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1608	258		
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of Subjects Responding to Pertussis PRN	92.16 (90.74 to 93.43)	91.09 (86.92 to 94.26)		

Statistical analyses

Statistical analysis title	Combined Lots A, B, C-Control Difference

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Combined Lot A, B, and C v Control

Number of subjects included in analysis	1866
Analysis specification	Pre-specified
Analysis type	non-inferiority[91]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.13
upper limit	5.47

Notes:

[91] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-10%.

Secondary: Percentage of Subjects Responding to Pertussis Fimbriae

End point title	Percentage of Subjects Responding to Pertussis Fimbriae

End point description:

Subject serum samples were collected for testing with an ELISA for antibodies to pertussis fimbriae. Sera response or endpoint was defined as follows: (1) if the predose titer was <4X LLOQ then the postdose titer was ≥4X LLOQ; (2) if the predose titer was ≥4X LLOQ then the postdose titer was ≥ the predose titer. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 4.

End point type	Secondary

End point timeframe:

Postdose 4 (Month 16)

End point values	Combined Lot A, B, and C	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1664	264		
Units: Percentage of subjects				
number (confidence interval 95%)				
Subjects Responding to Pertussis Fimbriae	92.97 (91.63 to 94.15)	90.15 (85.9 to 93.47)		

Statistical analyses

Statistical analysis title	Combined Lots A, B, C-Control Difference

Statistical analysis description:

Response rate analysis of Combined Lots A, B, and C-Control mean difference.

Comparison groups	Combined Lot A, B, and C v Control

Number of subjects included in analysis	1928
Analysis specification	Pre-specified
Analysis type	non-inferiority[92]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Mean difference (final values)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	7.4

Notes:

[92] - Response rate, response rate differences, and p-values were stratified by actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the response rates between any 2 lots was ≥-10%.

Secondary: Geometric Mean Concentrations (GMC) for Antibodies to Pneumococcal Serotypes

End point title	Geometric Mean Concentrations (GMC) for Antibodies to Pneumococcal Serotypes

End point description:

Subject serum samples were collected for testing with a multiplex electrochemiluminescence-based detection assay for serotype-specific pneumococcal polysaccharide antibodies. The analysis population included subjects who met the inclusion criteria, were not protocol violators, had an infant vaccination window of 42 to 84 days after the previous dose, and a blood draw sample window for the endpoint of 28 to 51 days after dose 3.

End point type	Secondary

End point timeframe:

Postdose 3 (Month 7)

End point values	Control	Combined Lot A, B, and C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	1256		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Pneumococcal Serotype 1 (n=191, 1256)	1.55 (1.39 to 1.73)	1.44 (1.38 to 1.5)		
Pneumococcal Serotype 3 (n=191, 1255)	0.5 (0.45 to 0.56)	0.48 (0.46 to 0.5)		
Pneumococcal Serotype 4 (n=189, 1255)	1.22 (1.1 to 1.35)	1.22 (1.17 to 1.27)		
Pneumococcal Serotype 5 (n=191, 1256)	1.61 (1.41 to 1.82)	1.49 (1.42 to 1.57)		
Pneumococcal Serotype 6A (n=191, 1251)	2.96 (2.64 to 3.32)	2.57 (2.45 to 2.69)		
Pneumococcal Serotype 6B (n=190, 1255)	1.29 (1.07 to 1.54)	1.01 (0.94 to 1.09)		
Pneumococcal Serotype 7F (n=191, 1256)	3.08 (2.77 to 3.41)	2.74 (2.64 to 2.85)		
Pneumococcal Serotype 9V (n=189, 1256)	1.35 (1.19 to 1.52)	1.35 (1.29 to 1.41)		

Pneumococcal Serotype 14 (n=191, 1256)	4.83 (4.26 to 5.48)	4.74 (4.48 to 5.01)		
Pneumococcal Serotype 18C (n=191, 1253)	1.82 (1.62 to 2.03)	1.62 (1.55 to 1.69)		
Pneumococcal Serotype 19A (n=191, 1254)	1.75 (1.55 to 1.99)	1.6 (1.53 to 1.68)		
Pneumococcal Serotype 19F (n=191, 1256)	2.26 (2.03 to 2.5)	2.18 (2.1 to 2.27)		
Pneumococcal Serotype 23F (n=190, 1254)	1.2 (1.04 to 1.38)	1.1 (1.04 to 1.16)		

Statistical analyses

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 1
Statistical analysis description:	
GMC ratio (Combined Lots A, B, C/Control)	
Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[93]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.04

Notes:

[93] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 3
Statistical analysis description:	
GMC ratio (Combined Lots A, B, C/Control)	
Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[94]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.06

Notes:

[94] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 4

Statistical analysis description:

GMC ratio (Combined Lots A, B, C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[95]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.12

Notes:

[95] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 5

Statistical analysis description:

GMC ratio (Combined Lots A, B, C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[96]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.07

Notes:

[96] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 6A

Statistical analysis description:

GMC ratio (Combined Lots A, B, C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[97]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	0.99

Notes:

[97] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 6B

Statistical analysis description:

GMC ratio (Combined Lots A, B, C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[98]
P-value	= 0.055
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.96

Notes:

[98] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 7F

Statistical analysis description:

GMC ratio (Combined Lots A, B, C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[99]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	0.99

Notes:

[99] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 9V

Statistical analysis description:

GMC ratio (Combined Lots A, B, C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[100]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.13

Notes:

[100] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 14

Statistical analysis description:

GMC ratio (Combined Lots A, B, C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[101]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.1

Notes:

[101] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory

variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 18C
Statistical analysis description:	
GMC ratio (Combined Lots A, B, C/Control)	
Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[102]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1

Notes:

[102] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 19A
Statistical analysis description:	
GMC ratio (Combined Lots A, B, C/Control)	
Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[103]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.03

Notes:

[103] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 19F
Statistical analysis description:	
GMC ratio (Combined Lots A, B, C/Control)	
Comparison groups	Control v Combined Lot A, B, and C

Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[104]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.08

Notes:

[104] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Statistical analysis title	Combined Lots A, B, C/Control Ratio; Serotype 23F

Statistical analysis description:

GMC ratio (Combined Lots A, B, C/Control)

Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	1447
Analysis specification	Pre-specified
Analysis type	non-inferiority[105]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	GMC Ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.06

Notes:

[105] - The estimates for GMC, GMC ratio, and p-values are based on an ANCOVA model with natural log-transformed postvaccination titer as the response variable, and vaccination group, natural log-transformed, prevaccination titer, actual brand of birth dose Hepatitis B vaccine as explanatory variables. Non-inferiority required that the lower limit of the 95% confidence interval of the GMC ratio is ≥0.67.

Secondary: Percentage of Subjects Reporting Solicited Injection-site and Systemic Reactions Within Five Days Following Any Infant Dose Vaccination in the V419 and Control Groups

End point title	Percentage of Subjects Reporting Solicited Injection-site and Systemic Reactions Within Five Days Following Any Infant Dose Vaccination in the V419 and Control Groups[106]

End point description:

Solicited injection site reactions: Pain, Erythema, and Swelling. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability. Grade 3 Solicited injection site reaction: Pain, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, >5 cm. Grade 3 Solicited systemic reactions: Fever (Pyrexia), ≥39.5°C rectal; Vomiting, ≥6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, >3 hours; Drowsiness (Somnolence), Sleeping most of the time or difficult to wake up; Appetite lost, Refuses ≥3 feeds or refuses most feeds; Irritability, Inconsolable.

End point type	Secondary

End point timeframe:

Day 0 up to Day 5 post-any infant dose vaccination

Notes:

[106] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: A descriptive analysis was performed for this outcome.

End point values	Control	Combined Lot A, B, and C		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	397	2390		
Units: Percentage of subjects				
number (not applicable)				
Any Injection site Erythema	40.8	44.6		
Severe Injection site Erythema	0.8	0.3		
Any Injection site Pain	72	70		
Severe Injection site Pain	5.5	6		
Any Injection site Swelling	34.5	34.5		
Severe Injection site Swelling	0.5	0.5		
Any Crying abnormal	72.5	74.8		
Severe Crying abnormal	12.6	9.5		
Any Decreased appetite	47.4	48.5		
Severe Decreased appetite	1.3	1.4		
Any Irritability	79.8	80.7		
Severe Irritability	6.5	7.8		
Any Pyrexia	33.2	47.1		
Severe Pyrexia	1.3	1.4		
Any Somnolence	73.3	73.2		
Severe Somnolence	3	3.5		
Any Vomiting	24.9	26.7		
Severe Vomiting	1.5	0.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Elevated Temperature By Severity Within Five Days Following Any Infant Dose Vaccination in the V419 and Control Groups

End point title	Percentage of Subjects With Elevated Temperature By Severity Within Five Days Following Any Infant Dose Vaccination in the V419 and Control Groups

End point description:

Maximum temperature (all routes) was based on actual temperatures recorded with no adjustments to the measurement route. Maximum temperature (rectal) was required of all subjects if the reading by another method was ≥38.0°C. Percentages were based on the number of subjects in the population with safety follow-up and temperature data.

End point type	Secondary

End point timeframe:

Day 0 up to Day 5 post-any Infant dose

End point values	Combined Lot A, B, and C	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2308	378		
Units: Percentage of subjects				
number (not applicable)				
Maximum temperature (all routes); <38.0°C	50.8	64.6		
Max. temp. (all routes); ≥38.0°C and <38.5°C; mild	27.2	23.3		
Max. (all routes); ≥38.5°C and <39.5°C; moderate	19.5	10.8		
Max. temp. (all routes); ≥39.5°C; severe	2.4	1.3		
Maximum temperature (rectal); <38.0°C	47.7	59		
Max. temp. (rectal); ≥38.0°C and <38.5°C; mild	26.5	23		
Max. temp. (rectal); ≥38.5°C and <39.5°C; moderate	19	10.6		
Max. temp. (rectal); ≥39.5°C; severe	2.4	1.3		

Statistical analyses

Statistical analysis title	Estimated Difference; All routes, <38°C
Statistical analysis description:	
The estimated difference was calculated for V419 group minus the Control group.	
Comparison groups	Control v Combined Lot A, B, and C
Number of subjects included in analysis	2686
Analysis specification	Pre-specified
Analysis type	other[107]
Parameter estimate	Mean difference (final values)
Point estimate	-13.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.8
upper limit	-8.4

Notes:

[107] - The 95% confidence intervals were based on the unstratified Miettinen and Nurminen method.

Statistical analysis title	Est. Difference; All routes, ≥38.5°C and <39.5°C
Statistical analysis description:	
The estimated difference was calculated for V419 group minus the Control group.	
Comparison groups	Combined Lot A, B, and C v Control

Number of subjects included in analysis	2686
Analysis specification	Pre-specified
Analysis type	other[108]
Parameter estimate	Mean difference (final values)
Point estimate	8.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.8
upper limit	11.9

Notes:

[108] - The 95% confidence intervals were based on the unstratified Miettinen and Nurminen method.

Statistical analysis title	Est. Difference; All routes, ≥38°C and <38.5°

Statistical analysis description:

The estimated difference was calculated for V419 group minus the Control group.

Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2686
Analysis specification	Pre-specified
Analysis type	other[109]
Parameter estimate	Mean difference (final values)
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	8.3

Notes:

[109] - The 95% confidence intervals were based on the unstratified Miettinen and Nurminen method.

Statistical analysis title	Est. Difference; All routes, ≥39.5°C

Statistical analysis description:

The estimated difference was calculated for V419 group minus the Control group.

Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2686
Analysis specification	Pre-specified
Analysis type	other[110]
Parameter estimate	Mean difference (final values)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	2.2

Notes:

[110] - The 95% confidence intervals were based on the unstratified Miettinen and Nurminen method.

Statistical analysis title	Estimated Difference; Rectal, <38°C

Statistical analysis description:

The estimated difference was calculated for V419 group minus the Control group.

Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2686
Analysis specification	Pre-specified
Analysis type	other[111]
Parameter estimate	Mean difference (final values)
Point estimate	-11.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.6
upper limit	-5.9

Notes:

[111] - The 95% confidence intervals were based on the unstratified Miettinen and Nurminen method.

Statistical analysis title	Estimated Difference; Rectal, ≥38°C and <38.5°C

Statistical analysis description:

The estimated difference was calculated for V419 group minus the Control group.

Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2686
Analysis specification	Pre-specified
Analysis type	other[112]
Parameter estimate	Mean difference (final values)
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	7.8

Notes:

[112] - The 95% confidence intervals were based on the unstratified Miettinen and Nurminen method.

Statistical analysis title	Estimated Difference; Rectal, ≥38.5°C and <39.5°C

Statistical analysis description:

The estimated difference was calculated for V419 group minus the Control group.

Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2686
Analysis specification	Pre-specified
Analysis type	other[113]
Parameter estimate	Mean difference (final values)
Point estimate	8.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.6
upper limit	11.6

Notes:

[113] - The 95% confidence intervals were based on the unstratified Miettinen and Nurminen method.

Statistical analysis title	Estimated Difference; Rectal, ≥39.5°C

Statistical analysis description:	
The estimated difference was calculated for V419 group minus the Control group.	
Comparison groups	Combined Lot A, B, and C v Control
Number of subjects included in analysis	2686
Analysis specification	Pre-specified
Analysis type	other[114]
Parameter estimate	Mean difference (final values)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	2.1

Notes:

[114] - The 95% confidence intervals were based on the unstratified Miettinen and Nurminen method.

Adverse events information

Timeframe for reporting adverse events:

SAEs: up to 6 months after vaccination 3 (the last infant vaccination) and up to 15 days after vaccination 4 (the toddler vaccination); Vaccine-related SAEs and deaths: up to Month 16 (duration of study); Other AEs: up to 15 days after any vaccination

Adverse event reporting additional description:

The All Subjects as Treated population included all randomized subjects who received at least one dose of study vaccine and had safety follow up. For safety analysis, subjects who received the 3 V419 lots were combined.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	V419 (Combined Lots A, B, and C)

Reporting group description:

V419 (Combined Lots A, B, and C) 0.5 mL intramuscular injection (IM) at 2, 4, 6 months of age; Pentacel™ 0.5 mL IM at 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; and RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age.

Reporting group title	Control

Reporting group description:

Pentacel™ 0.5 mL IM at 2, 4, 6, and 15 months of age; Prevnar13™ 0.5 mL IM at 2, 4, 6, and 15 months of age; RotaTeq™ 2 mL oral dose at 2, 4, and 6 months of age; and Modified Process Hepatitis B vaccine 0.5 mL IM at 2 and 6 months of age.

Serious adverse events	V419 (Combined Lots A, B, and C)	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	94 / 2390 (3.93%)	15 / 397 (3.78%)	
number of deaths (all causes)	5	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Brain contusion			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	3 / 2390 (0.13%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			

subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 2390 (0.00%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 2390 (0.00%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cyanosis			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumocephalus			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			

subjects affected / exposed	4 / 2390 (0.17%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 2390 (0.17%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	3 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden infant death syndrome			
subjects affected / exposed	2 / 2390 (0.08%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Death			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Irritability			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Idiopathic thrombocytopenic purpura			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	1 / 2390 (0.04%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 2390 (0.08%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 2390 (0.08%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal			

disorders			
Apnoeic attack			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial hyperreactivity			
subjects affected / exposed	2 / 2390 (0.08%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 2390 (0.00%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	2 / 2390 (0.08%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	12 / 2390 (0.50%)	4 / 397 (1.01%)	
occurrences causally related to treatment / all	0 / 12	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 2390 (0.04%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 2390 (0.13%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	2 / 2390 (0.08%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast abscess			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	9 / 2390 (0.38%)	3 / 397 (0.76%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cellulitis			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest wall abscess			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corona virus infection			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coxsackie viral infection			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	3 / 2390 (0.13%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema herpeticum			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	5 / 2390 (0.21%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	3 / 2390 (0.13%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin abscess			

subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			
subjects affected / exposed	2 / 2390 (0.08%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 2390 (0.08%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 2390 (0.00%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	5 / 2390 (0.21%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			

subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 2390 (0.00%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	4 / 2390 (0.17%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 2390 (0.04%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	3 / 2390 (0.13%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 2390 (0.00%)	2 / 397 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval abscess			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	2 / 2390 (0.08%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food intolerance			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	7 / 2390 (0.29%)	1 / 397 (0.25%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 2390 (0.04%)	0 / 397 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	V419 (Combined Lots A, B, and C)	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2259 / 2390 (94.52%)	371 / 397 (93.45%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	1816 / 2390 (75.98%)	298 / 397 (75.06%)	
occurrences (all)	4497	717	
General disorders and administration site conditions			
Crying			
subjects affected / exposed	1867 / 2390 (78.12%)	300 / 397 (75.57%)	
occurrences (all)	4597	763	
Irritability			
subjects affected / exposed	1993 / 2390 (83.39%)	324 / 397 (81.61%)	
occurrences (all)	5595	925	
Pyrexia			
subjects affected / exposed	1285 / 2390 (53.77%)	174 / 397 (43.83%)	
occurrences (all)	2302	274	
Injection site bruising			
subjects affected / exposed	128 / 2390 (5.36%)	22 / 397 (5.54%)	
occurrences (all)	174	31	
Injection site erythema			
subjects affected / exposed	1302 / 2390 (54.48%)	203 / 397 (51.13%)	
occurrences (all)	5189	911	
Injection site pain			
subjects affected / exposed	1883 / 2390 (78.79%)	314 / 397 (79.09%)	
occurrences (all)	8854	1815	
Injection site swelling			
subjects affected / exposed	1073 / 2390 (44.90%)	166 / 397 (41.81%)	
occurrences (all)	3652	687	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	192 / 2390 (8.03%)	23 / 397 (5.79%)	
occurrences (all)	215	24	
Vomiting			
subjects affected / exposed	723 / 2390 (30.25%)	110 / 397 (27.71%)	
occurrences (all)	1139	171	
Infections and infestations			
Otitis media			
subjects affected / exposed	147 / 2390 (6.15%)	39 / 397 (9.82%)	
occurrences (all)	162	44	
Upper respiratory tract infection			
subjects affected / exposed	276 / 2390 (11.55%)	48 / 397 (12.09%)	
occurrences (all)	306	54	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1355 / 2390 (56.69%)	217 / 397 (54.66%)	
occurrences (all)	2586	402	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 March 2011	Evaluation of lot consistency was revised to be based on GMTs, rather than response rates, at 1 month after the third dose of PR5I/Control, analysis of lot consistency based on response rates was moved from a conditional primary hypothesis to Secondary Hypothesis #1, a non-inferiority analysis of PR5I to Control was added as Secondary Hypothesis #3, statistical criterion for the evaluation of the immunogenicity of Prevnar13™ was revised, objectives and hypotheses were renumbered accordingly, sponsor name was updated to Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., all references to Interactive Voice Response System was updated to Interactive Response Technology, and the reference list was reorganized to present references sequentially.
24 January 2013	Added a new primary statistical analysis method for all GMT analyses to account for missing baseline titers due to limited serum volumes obtained from 2-month old infant subjects at study entry, added a second Per Protocol population (referred to as Per Protocol-Revised Window) in addition to the existing Per Protocol population (Per Protocol-Original Window) to account for subjects who received study vaccinations and/or blood draws outside of narrow protocol-defined visit windows, and added 2 sensitivity analyses: (1) analysis of GMT endpoints with no baseline adjustment and (2) analysis of GMT endpoints based on data from subjects with both baseline and post vaccination titers to support the ANCOVA with multiple imputation for missing baseline titers primary analysis for GMT endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported