Clinical trial results:
A Phase 2, randomized,controlled, observer-Blinded study conducted to describe the immunogenicity, safety, and tolerability of a Neisseria meningitidis Serogroup B Bivalent Recombinant Lipoprotein 2086 Vaccine (Bivalent rLP2086) when administered to healthy toddlers Aged 12 to <18 Months or 18 to <24 Months

Summary

EudraCT number	2011-004400-38
Trial protocol	CZ PL FI
Global end of trial date	

Results information

Result version number	v2
This version publication date	27 September 2020
First version publication date	09 March 2018
Version creation reason	• New data added to full data set • Correction of full data set Correction / Update

Trial information

Trial identification

Sponsor protocol code	B1971035

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02534935
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 110017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001037-PIP02-11
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	Interim
Date of interim/final analysis	26 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 August 2017
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the immune response as measured by hSBA performed with 4 primary MnB strains, 2 expressing an LP2086 subfamily A protein and 2 expressing an LP2086 subfamily B protein, measured 1 month after the third vaccination with bivalent rLP2086,in healthy toddlers aged 12 to <18 months and healthy toddlers aged 18 to <24 months at study entry and also to evaluate the safety profile of bivalent rLP2086 compared to a control (hepatitis A virus [HAV] vaccine), as measured by local reactions, systemic events, adverse events (AEs), serious adverse events (SAEs), newly diagnosed chronic medical conditions (NDCMCs), medically attended events (MAEs), and immediate AEs in healthy toddlers 12 to <18 months and 18 to <24 months of age at study entry, and in both age strata combined.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 August 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 118
Country: Number of subjects enrolled	Czech Republic: 100
Country: Number of subjects enrolled	Finland: 26
Country: Number of subjects enrolled	Poland: 152
Worldwide total number of subjects	396
EEA total number of subjects	278

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	396
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: -

Pre-assignment

Screening details:

A total of 396 subjects were enrolled at multiple centers in four countries in the study.

Period 1

Period 1 title	Stage 1 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)

Arm description:

Subjects from greater than or equal to (>=) 12 months to less than (<) 24 months of age, received intramuscular injection of 60 microgram (µg) of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.

Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 0.5 milliliter (mL) bivalent rLP2086 as intramuscular injection at Months 0, 2, and 6.

Arm title	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)

Arm description:

Subjects from >=12 months to <24 months of age, received intramuscular injection of 120 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.

Arm type	Experimental
Investigational medicinal product name	Bivalent rLP2086
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 0.5 mL bivalent rLP2086 as intramuscular injection at Months 0, 2, and 6.

Arm title	Group 3: HAV/Saline (>=12 months to <24 months)

Arm description:

Subjects from >=12 months to <24 months of age, received intramuscular injection of saline on 2-month and HAV vaccine on a 0-, 6- month schedule.

Arm type	Active comparator

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

Dosage and administration details:

Subjects were administered 0.5 mL HAV vaccine as intramuscular injection at Months 0 and 6.

Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 0.5 mL saline solution as intramuscular injection at Month 2.

Number of subjects in period 1	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)
Started	44	220	132
Completed	44	210	127
Not completed	0	10	5
Consent withdrawn by subject	-	3	3
Adverse event, non-fatal	-	2	-
No longer meets the eligibility criteria	-	3	-
No longer willing to participate	-	1	1
Lost to follow-up	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)
Reporting group description:	
Subjects from greater than or equal to (>=) 12 months to less than (<) 24 months of age, received intramuscular injection of 60 microgram (µg) of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)
Reporting group description:	
Subjects from >=12 months to <24 months of age, received intramuscular injection of 120 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 3: HAV/Saline (>=12 months to <24 months)
Reporting group description:	
Subjects from >=12 months to <24 months of age, received intramuscular injection of saline on 2-month and HAV vaccine on a 0-, 6- month schedule.	

Reporting group values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)
Number of subjects	44	220	132
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)	44	220	132
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: years			
arithmetic mean	16.9	17.4	17.3
standard deviation	± 4.08	± 3.54	± 3.58
Sex: Female, Male Units: Subjects			
Female	21	115	74
Male	23	105	58
Race/Ethnicity, Customized Units: Subjects			
Race: White|	37	210	127
Race: Asian|	5	2	1
Race: Other|	2	8	4
Race/Ethnicity, Customized Units: Subjects			

Ethinicity: Hispanic|	0	2	0
Ethinicity: Non-Hispanic|	44	218	132

Reporting group values	Total		
Number of subjects	396		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	396		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	210		
Male	186		
Race/Ethnicity, Customized Units: Subjects			
Race: White|	374		
Race: Asian|	8		
Race: Other|	14		
Race/Ethnicity, Customized Units: Subjects			
Ethinicity: Hispanic|	2		
Ethinicity: Non-Hispanic|	394		

End points

End points reporting groups

Reporting group title	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)
Reporting group description:	
Subjects from greater than or equal to (>=) 12 months to less than (<) 24 months of age, received intramuscular injection of 60 microgram (µg) of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)
Reporting group description:	
Subjects from >=12 months to <24 months of age, received intramuscular injection of 120 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 3: HAV/Saline (>=12 months to <24 months)
Reporting group description:	
Subjects from >=12 months to <24 months of age, received intramuscular injection of saline on 2-month and HAV vaccine on a 0-, 6- month schedule.	
Subject analysis set title	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects from >=12 months to <18 months of age, received intramuscular injection of 60 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Subject analysis set title	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects from >=18 months to <24 months of age, received intramuscular injection of 60 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Subject analysis set title	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects from >=12 months to <18 months of age, received intramuscular injection of 120 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Subject analysis set title	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects from >=18 months to <24 months of age, received intramuscular injection of 120 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.	
Subject analysis set title	Group 3: HAV/Saline (>=12 months to <18 months)
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects from >=12 months to <18 months of age, received intramuscular injection of saline on 2-month and HAV vaccine on a 0-, 6- month schedule.	
Subject analysis set title	Group 3: HAV/Saline (>=18 months to <24 months)
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects from >=18 months to <24 months of age, received intramuscular injection of saline on 2-month and HAV vaccine on a 0-, 6- month schedule.	
Subject analysis set title	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects from >=12 months to <18 months of age, received intramuscular injection of 60 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.

Subject analysis set title	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects from >=18 months to <24 months of age, received intramuscular injection of 60 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.

Subject analysis set title	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects from >=12 months to <18 months of age, received intramuscular injection of 120 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.

Subject analysis set title	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects from >=18 months to <24 months of age, received intramuscular injection of 120 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.

Subject analysis set title	Group 3: HAV/Saline (>=12 months to <18 months)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects from >=12 months to <18 months of age, received intramuscular injection of saline on 2-month and HAV vaccine on a 0-, 6- month schedule.

Subject analysis set title	Group 3: HAV/Saline (>=18 months to <24 months)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects from >=18 months to <24 months of age, received intramuscular injection of saline on 2-month and HAV vaccine on a 0-, 6- month schedule.

Primary: Percentage of Subjects With Serum Bactericidal Assay Using Human Complement (hSBA) Titers >= Lower Limit of Quantitation (LLOQ) for Each of the 4 Primary Neisseria Meningitidis Serogroup B (MnB) Test Strains 1 Month After Vaccination 3

End point title	Percentage of Subjects With Serum Bactericidal Assay Using Human Complement (hSBA) Titers >= Lower Limit of Quantitation (LLOQ) for Each of the 4 Primary Neisseria Meningitidis Serogroup B (MnB) Test Strains 1 Month After Vaccination 3[1]

End point description:

Percentage of subjects achieving hSBA titer >= LLOQ were computed along with corresponding 2-sided 95 percent (%) confidence interval (CIs). LLOQ was 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24) and PMB2707 (B44). All eligible subjects randomized to study received,scheduled investigational products, had pre and post vaccination blood drawn with valid and determinate assay results and had no important protocol deviation.Here,Overall number of subjects analyzed(N) signifies subjects evaluable for this endpoint and n signifies number of subjects analyzed at specific time points only.

End point type	Primary

End point timeframe:

1 month after vaccination 3

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	11	47	51
Units: percentage of subjects				
number (confidence interval 95%)				
PMB80 [A22]| (n =9, 11, 45, 51, 31, 29)	88.9 (51.8 to 99.7)	90.9 (58.7 to 99.8)	91.1 (78.8 to 97.5)	88.2 (76.1 to 95.6)
PMB2001 [A56]| (n =9, 10, 47, 48, 24, 30)	100.0 (66.4 to 100.0)	100.0 (69.2 to 100.0)	100.0 (92.5 to 100.0)	100.0 (92.6 to 100.0)
PMB2948 [B24]| (n =9, 11, 45, 50, 31, 29)	88.9 (51.8 to 99.7)	81.8 (48.2 to 97.7)	71.1 (55.7 to 83.6)	72.0 (57.5 to 83.8)
PMB2707 [B44]| (n =9, 10, 47, 47, 24, 30)	88.9 (51.8 to 99.7)	90.0 (55.5 to 99.7)	87.2 (74.3 to 95.2)	85.1 (71.7 to 93.8)

End point values	Group 3: HAV/Saline (>=12 months to <18 months)	Group 3: HAV/Saline (>=18 months to <24 months)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	31	30		
Units: percentage of subjects				
number (confidence interval 95%)				
PMB80 [A22]| (n =9, 11, 45, 51, 31, 29)	3.2 (0.1 to 16.7)	6.9 (0.8 to 22.8)		
PMB2001 [A56]| (n =9, 10, 47, 48, 24, 30)	0.0 (0.0 to 14.2)	3.3 (0.1 to 17.2)		
PMB2948 [B24]| (n =9, 11, 45, 50, 31, 29)	3.2 (0.1 to 16.7)	6.9 (0.8 to 22.8)		
PMB2707 [B44]| (n =9, 10, 47, 47, 24, 30)	0.0 (0.0 to 14.2)	0.0 (0.0 to 11.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Pre-specified Local Reactions Within 7 Days After Vaccination 1

End point title	Percentage of Subjects Reporting Pre-specified Local Reactions Within 7 Days After Vaccination 1[2]

End point description:

Local reactions included tenderness at injection site, swelling and redness collected by using an e-diary. Tenderness was graded as: mild (hurted if gently touched), moderate (hurted if gently touched with crying) and severe (caused limitation of limb movement). Redness and swelling were graded as: mild (0.5-2.0 cm), moderate (2.5 to 7.0 cm) and severe (>7.0 cm). Safety population: all subjects who received at least 1 dose of an investigational product (rLP2086 or HAV vaccine) and had safety data available.

End point type	Primary

End point timeframe:

within 7 Days after Vaccination 1

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44[3]	220[4]	132[5]	22[6]
Units: percentage of subjects				
number (confidence interval 95%)				
Tenderness at injection site: Any|	59.1 (43.2 to 73.7)	57.7 (50.9 to 64.3)	17.4 (11.4 to 25.0)	68.2 (45.1 to 86.1)
Tenderness at injection site: Mild|	36.4 (22.4 to 52.2)	30.9 (24.9 to 37.5)	15.9 (10.1 to 23.3)	45.5 (24.4 to 67.8)
Tenderness at injection site: Moderate|	20.5 (9.8 to 35.3)	22.7 (17.4 to 28.8)	1.5 (0.2 to 5.4)	22.7 (7.8 to 45.4)
Tenderness at injection site: Severe|	2.3 (0.1 to 12.0)	4.1 (1.9 to 7.6)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Redness: Any|	54.5 (38.8 to 69.6)	46.8 (40.1 to 53.6)	15.2 (9.5 to 22.4)	68.2 (45.1 to 86.1)
Redness: Mild|	34.1 (20.5 to 49.9)	28.6 (22.8 to 35.1)	15.2 (9.5 to 22.4)	40.9 (20.7 to 63.6)
Redness: Moderate|	20.5 (9.8 to 35.3)	16.8 (12.1 to 22.4)	0.0 (0.0 to 2.8)	27.3 (10.7 to 50.2)
Redness: Severe|	0.0 (0.0 to 8.0)	1.4 (0.3 to 3.9)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Swelling: Any|	29.5 (16.8 to 45.2)	28.6 (22.8 to 35.1)	9.8 (5.3 to 16.3)	36.4 (17.2 to 59.3)
Swelling: Mild|	18.2 (8.2 to 32.7)	17.3 (12.5 to 22.9)	9.8 (5.3 to 16.3)	22.7 (7.8 to 45.4)
Swelling: Moderate|	11.4 (3.8 to 24.6)	10.9 (7.1 to 15.8)	0.0 (0.0 to 2.8)	13.6 (2.9 to 34.9)
Swelling: Severe|	0.0 (0.0 to 8.0)	0.5 (0.0 to 2.5)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)

Notes:

[3] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[4] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[5] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[6] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[7]	110[8]	110[9]	66[10]
Units: percentage of subjects				
number (confidence interval 95%)				
Tenderness at injection site: Any|	50.0 (28.2 to 71.8)	50.9 (41.2 to 60.6)	64.5 (54.9 to 73.4)	15.2 (7.5 to 26.1)
Tenderness at injection site: Mild|	27.3 (10.7 to 50.2)	27.3 (19.2 to 36.6)	34.5 (25.7 to 44.2)	12.1 (5.4 to 22.5)

Tenderness at injection site: Moderate|	18.2 (5.2 to 40.3)	20.9 (13.7 to 29.7)	24.5 (16.8 to 33.7)	3.0 (0.4 to 10.5)
Tenderness at injection site: Severe|	4.5 (0.1 to 22.8)	2.7 (0.6 to 7.8)	5.5 (2.0 to 11.5)	0.0 (0.0 to 5.4)
Redness: Any|	40.9 (20.7 to 63.6)	50.9 (41.2 to 60.6)	42.7 (33.3 to 52.5)	13.6 (6.4 to 24.3)
Redness: Mild|	27.3 (10.7 to 50.2)	35.5 (26.6 to 45.1)	21.8 (14.5 to 30.7)	13.6 (6.4 to 24.3)
Redness: Moderate|	13.6 (2.9 to 34.9)	14.5 (8.5 to 22.5)	19.1 (12.2 to 27.7)	0.0 (0.0 to 5.4)
Redness: Severe|	0.0 (0.0 to 15.4)	0.9 (0.0 to 5.0)	1.8 (0.2 to 6.4)	0.0 (0.0 to 5.4)
Swelling: Any|	22.7 (7.8 to 45.4)	30.0 (21.6 to 39.5)	27.3 (19.2 to 36.6)	7.6 (2.5 to 16.8)
Swelling: Mild|	13.6 (2.9 to 34.9)	15.5 (9.3 to 23.6)	19.1 (12.2 to 27.7)	7.6 (2.5 to 16.8)
Swelling: Moderate|	9.1 (1.1 to 29.2)	13.6 (7.8 to 21.5)	8.2 (3.8 to 15.0)	0.0 (0.0 to 5.4)
Swelling: Severe|	0.0 (0.0 to 15.4)	0.9 (0.0 to 5.0)	0.0 (0.0 to 3.3)	0.0 (0.0 to 5.4)

Notes:

[7] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[8] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[9] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[10] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	66[11]			
Units: percentage of subjects				
number (confidence interval 95%)				
Tenderness at injection site: Any|	19.7 (10.9 to 31.3)			
Tenderness at injection site: Mild|	19.7 (10.9 to 31.3)			
Tenderness at injection site: Moderate|	0.0 (0.0 to 5.4)			
Tenderness at injection site: Severe|	0.0 (0.0 to 5.4)			
Redness: Any|	16.7 (8.6 to 27.9)			
Redness: Mild|	16.7 (8.6 to 27.9)			
Redness: Moderate|	0.0 (0.0 to 5.4)			
Redness: Severe|	0.0 (0.0 to 5.4)			
Swelling: Any|	12.1 (5.4 to 22.5)			
Swelling: Mild|	12.1 (5.4 to 22.5)			
Swelling: Moderate|	0.0 (0.0 to 5.4)			
Swelling: Severe|	0.0 (0.0 to 5.4)			

Notes:

[11] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Pre-specified Local Reactions Within 7 Days After Vaccination 2

End point title	Percentage of Subjects Reporting Pre-specified Local Reactions Within 7 Days After Vaccination 2[12]

End point description:

Local reactions included tenderness at injection site, swelling and redness collected by using an e-diary. Tenderness was graded as: mild (hurted if gently touched), moderate (hurted if gently touched with crying) and severe (caused limitation of limb movement). Redness and swelling were graded as: mild (0.5-2.0 cm), moderate (2.5 to 7.0 cm) and severe (>7.0 cm). Safety population: all subjects who received at least 1 dose of an investigational product (rLP2086 or HAV vaccine) and had safety data available. Here, N (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

within 7 Days after Vaccination 2

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44[13]	212[14]	128[15]	22[16]
Units: percentage of subjects				
number (confidence interval 95%)				
Tenderness at injection site: Any|	47.7 (32.5 to 63.3)	53.3 (46.3 to 60.2)	14.8 (9.2 to 22.2)	45.5 (24.4 to 67.8)
Tenderness at injection site: Mild|	36.4 (22.4 to 52.2)	32.1 (25.8 to 38.8)	14.1 (8.6 to 21.3)	31.8 (13.9 to 54.9)
Tenderness at injection site: Moderate|	11.4 (3.8 to 24.6)	18.4 (13.4 to 24.3)	0.8 (0.0 to 4.3)	13.6 (2.9 to 34.9)
Tenderness at injection site: Severe|	0.0 (0.0 to 8.0)	2.8 (1.0 to 6.1)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Redness: Any|	40.9 (26.3 to 56.8)	35.8 (29.4 to 42.7)	7.8 (3.8 to 13.9)	50.0 (28.2 to 71.8)
Redness: Mild|	34.1 (20.5 to 49.9)	22.6 (17.2 to 28.9)	7.8 (3.8 to 13.9)	40.9 (20.7 to 63.6)
Redness: Moderate|	6.8 (1.4 to 18.7)	13.2 (9.0 to 18.5)	0.0 (0.0 to 2.8)	9.1 (1.1 to 29.2)
Redness: Severe|	0.0 (0.0 to 8.0)	0.0 (0.0 to 1.7)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Swelling: Any|	22.7 (11.5 to 37.8)	20.3 (15.1 to 26.3)	4.7 (1.7 to 9.9)	18.2 (5.2 to 40.3)
Swelling: Mild|	15.9 (6.6 to 30.1)	13.7 (9.4 to 19.1)	4.7 (1.7 to 9.9)	18.2 (5.2 to 40.3)
Swelling: Moderate|	6.8 (1.4 to 18.7)	6.1 (3.3 to 10.3)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Swelling: Severe|	0.0 (0.0 to 8.0)	0.5 (0.0 to 2.6)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)

Notes:

[13] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

[14] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[15] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[16] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[17]	105[18]	107[19]	63[20]
Units: percentage of subjects				
number (confidence interval 95%)				
Tenderness at injection site: Any|	50.0 (28.2 to 71.8)	45.7 (36.0 to 55.7)	60.7 (50.8 to 70.0)	14.3 (6.7 to 25.4)
Tenderness at injection site: Mild|	40.9 (20.7 to 63.6)	31.4 (22.7 to 41.2)	32.7 (24.0 to 42.5)	12.7 (5.6 to 23.5)
Tenderness at injection site: Moderate|	9.1 (1.1 to 29.2)	12.4 (6.8 to 20.0)	22.5 (16.5 to 24.3)	1.6 (0.0 to 8.5)
Tenderness at injection site: Severe|	0.0 (0.0 to 15.4)	1.9 (0.2 to 6.7)	3.7 (1.0 to 9.3)	0.0 (0.0 to 5.7)
Redness: Any|	31.8 (13.9 to 54.9)	33.3 (24.4 to 43.2)	38.3 (29.1 to 48.2)	6.3 (1.8 to 15.5)
Redness: Mild|	27.3 (10.7 to 50.2)	21.9 (14.4 to 31.0)	23.4 (15.7 to 32.5)	6.3 (1.8 to 15.5)
Redness: Moderate|	4.5 (0.1 to 22.8)	11.4 (6.0 to 19.1)	15.0 (8.8 to 23.1)	0.0 (0.0 to 5.7)
Redness: Severe|	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.5)	0.0 (0.0 to 3.4)	0.0 (0.0 to 5.7)
Swelling: Any|	27.3 (10.7 to 50.2)	21.0 (13.6 to 30.0)	19.6 (12.6 to 28.4)	1.6 (0.0 to 8.5)
Swelling: Mild|	13.6 (2.9 to 34.9)	14.3 (8.2 to 22.5)	13.1 (7.3 to 21.0)	1.6 (0.0 to 8.5)
Swelling: Moderate|	13.6 (2.9 to 34.9)	6.7 (2.7 to 13.3)	5.6 (2.1 to 11.8)	0.0 (0.0 to 5.7)
Swelling: Severe|	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.5)	0.9 (0.0 to 5.1)	0.0 (0.0 to 5.7)

Notes:
[17] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[18] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[19] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[20] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	65[21]			
Units: percentage of subjects				
number (confidence interval 95%)				
Tenderness at injection site: Any|	15.4 (7.6 to 26.5)			

Tenderness at injection site: Mild|	15.4 (7.6 to 26.5)			
Tenderness at injection site: Moderate|	0.0 (0.0 to 5.5)			
Tenderness at injection site: Severe|	0.0 (0.0 to 5.5)			
Redness: Any|	9.2 (3.5 to 19.0)			
Redness: Mild|	9.2 (3.5 to 19.0)			
Redness: Moderate|	0.0 (0.0 to 5.5)			
Redness: Severe|	0.0 (0.0 to 5.5)			
Swelling: Any|	7.7 (2.5 to 17.0)			
Swelling: Mild|	7.7 (2.5 to 17.0)			
Swelling: Moderate|	0.0 (0.0 to 5.5)			
Swelling: Severe|	0.0 (0.0 to 5.5)			

Notes:

[21] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Pre-specified Local Reactions Within 7 Days After Vaccination 3

End point title	Percentage of Subjects Reporting Pre-specified Local Reactions Within 7 Days After Vaccination 3[22]

End point description:

Local reactions included tenderness at injection site, swelling and redness collected by using an e-diary. Tenderness was graded as: mild (hurted if gently touched), moderate (hurted if gently touched with crying) and severe (caused limitation of limb movement). Redness and swelling were graded as: mild (0.5-2.0 cm), moderate (2.5 to 7.0 cm) and severe (>7.0 cm). Safety population: all subjects who received at least 1 dose of an investigational product (rLP2086 or HAV vaccine) and had safety data available. Here, N signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

within 7 Days after Vaccination 3

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44[23]	212[24]	128[25]	22[26]
Units: percentage of subjects				
number (confidence interval 95%)				
Tenderness at injection site: Any|	56.8 (41.0 to 71.7)	57.1 (50.1 to 63.8)	15.6 (9.8 to 23.1)	54.5 (32.2 to 75.6)
Tenderness at injection site: Mild|	31.8 (18.6 to 47.6)	32.1 (25.8 to 38.8)	12.5 (7.3 to 19.5)	22.7 (7.8 to 45.4)
Tenderness at injection site: Moderate|	25.0 (13.2 to 40.3)	19.8 (14.7 to 25.8)	3.1 (0.9 to 7.8)	31.8 (13.9 to 54.9)

Tenderness at injection site: Severe|	0.0 (0.0 to 8.0)	5.2 (2.6 to 9.1)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Redness: Any|	38.6 (24.4 to 54.5)	33.0 (26.7 to 39.8)	7.8 (3.8 to 13.9)	40.9 (20.7 to 63.6)
Redness: Mild|	29.5 (16.8 to 45.2)	20.8 (15.5 to 26.8)	7.0 (3.3 to 12.9)	31.8 (13.9 to 54.9)
Redness: Moderate|	9.1 (2.5 to 21.7)	11.8 (7.8 to 16.9)	0.8 (0.0 to 4.3)	9.1 (1.1 to 29.2)
Redness: Severe|	0.0 (0.0 to 8.0)	0.5 (0.0 to 2.6)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Swelling: Any|	22.7 (11.5 to 37.8)	22.6 (17.2 to 28.9)	5.5 (2.2 to 10.9)	18.2 (5.2 to 40.3)
Swelling: Mild|	11.4 (3.8 to 24.6)	13.7 (9.4 to 19.1)	4.7 (1.7 to 9.9)	9.1 (1.1 to 29.2)
Swelling: Moderate|	11.4 (3.8 to 24.6)	8.5 (5.1 to 13.1)	0.8 (0.0 to 4.3)	9.1 (1.1 to 29.2)
Swelling: Severe|	0.0 (0.0 to 8.0)	0.5 (0.0 to 2.6)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)

Notes:

[23] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[24] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[25] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[26] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[27]	104[28]	108[29]	65[30]
Units: percentage of subjects				
number (confidence interval 95%)				
Tenderness at injection site: Any|	59.1 (36.4 to 79.3)	51.9 (41.9 to 61.8)	62.0 (52.2 to 71.2)	16.9 (8.8 to 28.3)
Tenderness at injection site: Mild|	40.9 (20.7 to 63.6)	29.8 (21.2 to 39.6)	34.3 (25.4 to 44)	12.3 (5.5 to 22.8)
Tenderness at injection site: Moderate|	18.2 (5.2 to 40.3)	17.3 (10.6 to 26.0)	22.2 (14.8 to 31.2)	4.6 (1.0 to 12.9)
Tenderness at injection site: Severe|	0.0 (0.0 to 15.4)	4.8 (1.6 to 10.9)	5.6 (2.1 to 11.7)	0.0 (0.0 to 5.5)
Redness: Any|	36.4 (17.2 to 59.3)	32.7 (23.8 to 42.6)	33.3 (24.6 to 43.1)	7.7 (2.5 to 17.0)
Redness: Mild|	27.3 (10.7 to 50.2)	23.1 (15.4 to 32.4)	18.5 (11.7 to 27.1)	6.2 (1.7 to 15.0)
Redness: Moderate|	9.1 (1.1 to 29.2)	8.7 (4.0 to 15.8)	14.8 (8.7 to 22.9)	1.5 (0.0 to 8.3)
Redness: Severe|	0.0 (0.0 to 15.4)	1.0 (0.0 to 5.2)	0.0 (0.0 to 3.4)	0.0 (0.0 to 5.5)
Swelling: Any|	27.3 (10.7 to 50.2)	23.1 (15.4 to 32.4)	22.2 (14.8 to 31.2)	4.6 (1.0 to 12.9)
Swelling: Mild|	13.6 (2.9 to 34.9)	16.3 (9.8 to 24.9)	11.1 (5.9 to 18.6)	4.6 (1.0 to 12.9)
Swelling: Moderate|	13.6 (2.9 to 34.9)	5.8 (2.1 to 12.1)	11.1 (5.9 to 18.6)	0.0 (0.0 to 5.5)
Swelling: Severe|	0.0 (0.0 to 15.4)	1.0 (0.0 to 5.2)	0.0 (0.0 to 3.4)	0.0 (0.0 to 5.5)

Notes:

[27] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[28] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[29] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[30] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	63[31]			
Units: percentage of subjects				
number (confidence interval 95%)				
Tenderness at injection site: Any|	14.3 (6.7 to 25.4)			
Tenderness at injection site: Mild|	12.7 (5.6 to 23.5)			
Tenderness at injection site: Moderate|	1.6 (0.0 to 8.5)			
Tenderness at injection site: Severe|	0.0 (0.0 to 5.7)			
Redness: Any|	7.9 (2.6 to 17.6)			
Redness: Mild|	7.9 (2.6 to 17.6)			
Redness: Moderate|	0.0 (0.0 to 5.7)			
Redness: Severe|	0.0 (0.0 to 5.7)			
Swelling: Any|	6.3 (1.8 to 15.5)			
Swelling: Mild|	4.8 (1.0 to 13.3)			
Swelling: Moderate|	1.6 (0.0 to 8.5)			
Swelling: Severe|	0.0 (0.0 to 5.7)			

Notes:

[31] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 1

End point title	Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 1[32]

End point description:

Systemic reactions included fever, irritability, drowsiness, loss of or decreased appetite and recorded by using an e-diary. Fever was graded as 38.0 to 38.4 degree Celsius (C), 38.5 to 38.9 degree C, 39.0 to 39.4 degree C, >39.5 to 40.0 degree C and >40.0 degree C. Irritability was graded as mild (easily consolable), moderate (requiring increased attention) and severe (inconsolable). Drowsiness was graded as mild (Increased or prolonged sleeping bouts), moderate (slightly subdued interfering with daily activity) and severe (disabling not interested in usual daily activity). Loss of or decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Safety population: all subjects who received at least 1 dose of an investigational product (rLP2086 or HAV vaccine) and had safety data available.

End point type	Primary

End point timeframe:

within 7 Days after Vaccination 1

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44[33]	220[34]	132[35]	22[36]
Units: percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C|	36.4 (22.4 to 52.2)	27.7 (21.9 to 34.1)	6.1 (2.7 to 11.6)	40.9 (20.7 to 63.6)
Fever 38 to <38.5 degrees C|	20.5 (9.8 to 35.3)	7.3 (4.2 to 11.5)	3.8 (1.2 to 8.6)	22.7 (7.8 to 45.4)
Fever 38.5 to <39 degrees C|	11.4 (3.8 to 24.6)	14.1 (9.8 to 19.4)	0.8 (0.0 to 4.1)	13.6 (2.9 to 34.9)
Fever 39 to <39.5 degrees C|	0.0 (0.0 to 8.0)	4.1 (1.9 to 7.6)	1.5 (0.2 to 5.4)	0.0 (0.0 to 15.4)
Fever 39.5 to <=40 degrees C|	4.5 (0.6 to 15.5)	1.8 (0.5 to 4.6)	0.0 (0.0 to 2.8)	4.5 (0.1 to 22.8)
Fever >40 degrees C|	0.0 (0.0 to 8.0)	0.5 (0.0 to 2.5)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Irritability: Any|	56.8 (41.0 to 71.7)	66.4 (59.7 to 72.6)	37.1 (28.9 to 46.0)	63.6 (40.7 to 82.8)
Irritability: Mild|	18.2 (8.2 to 32.7)	17.7 (12.9 to 23.4)	12.1 (7.1 to 18.9)	27.3 (10.7 to 50.2)
Irritability: Moderate|	36.4 (22.4 to 52.2)	42.7 (36.1 to 49.6)	23.5 (16.5 to 31.6)	31.8 (13.9 to 54.9)
Irritability: Severe|	2.3 (0.1 to 12.0)	5.9 (3.2 to 9.9)	1.5 (0.2 to 5.4)	4.5 (0.1 to 22.8)
Drowsiness: Any|	43.2 (28.3 to 59.0)	44.1 (37.4 to 50.9)	18.2 (12.0 to 25.8)	45.5 (24.4 to 67.8)
Drowsiness: Mild|	34.1 (20.5 to 49.9)	26.4 (20.7 to 32.7)	11.4 (6.5 to 18.0)	36.4 (17.2 to 59.3)
Drowsiness: Moderate|	9.1 (2.5 to 21.7)	13.6 (9.4 to 18.9)	6.1 (2.7 to 11.6)	9.1 (1.1 to 29.2)
Drowsiness: Severe|	0.0 (0.0 to 8.0)	4.1 (1.9 to 7.6)	0.8 (0.0 to 4.1)	0.0 (0.0 to 15.4)
Loss of or decrease appetite: Any|	36.4 (22.4 to 52.2)	45.5 (38.7 to 52.3)	22.7 (15.9 to 30.8)	36.4 (17.2 to 59.3)
Loss of or decrease appetite: Mild|	20.5 (9.8 to 35.3)	20.5 (15.3 to 26.4)	10.6 (5.9 to 17.2)	22.7 (7.8 to 45.4)
Loss of or decrease appetite: Moderate|	11.4 (3.8 to 24.6)	20.0 (14.9 to 25.9)	9.8 (5.3 to 16.3)	13.6 (2.9 to 34.9)
Loss of or decrease appetite: Severe|	4.5 (0.6 to 15.5)	5.0 (2.5 to 8.8)	2.3 (0.5 to 6.5)	0.0 (0.0 to 15.4)
Antipyretic medication use|	52.3 (36.7 to 67.5)	46.8 (40.1 to 53.6)	19.7 (13.3 to 27.5)	45.5 (24.4 to 67.8)

Notes:

[33] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[34] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[35] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[36] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

End point values	Group 1: 60-µg bivalent	Group 2: 120-µg bivalent	Group 2: 120-µg bivalent	Group 3: HAV/Saline

	rLP2086 (>=18 months to <24 months)	rLP2086 (>=12 months to <18 months)	rLP2086 (>=18 months to <24 months)	(>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[37]	110[38]	110[39]	66[40]
Units: percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C|	31.8 (13.9 to 54.9)	28.2 (20.0 to 37.6)	27.3 (19.2 to 36.6)	10.6 (4.4 to 20.6)
Fever 38 to <38.5 degrees C|	18.2 (5.2 to 40.3)	7.3 (3.2 to 13.8)	7.3 (3.2 to 13.8)	6.1 (1.7 to 14.8)
Fever 38.5 to <39 degrees C|	9.1 (1.1 to 29.2)	14.5 (8.5 to 22.5)	13.6 (7.8 to 21.5)	1.5 (0.0 to 8.2)
Fever 39 to <39.5 degrees C|	0.0 (0.0 to 15.4)	4.5 (1.5 to 10.3)	3.6 (1.0 to 9.0)	3.0 (0.4 to 10.5)
Fever 39.5 to <=40 degrees C|	4.5 (0.1 to 22.8)	1.8 (0.2 to 6.4)	1.8 (0.2 to 6.4)	0.0 (0.0 to 5.4)
Fever >40 degrees C|	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.3)	0.9 (0.0 to 5.0)	0.0 (0.0 to 5.4)
Irritability: Any|	50.0 (28.2 to 71.8)	71.8 (62.4 to 80.0)	60.9 (51.1 to 70.1)	40.9 (29.0 to 53.7)
Irritability: Mild|	9.1 (1.1 to 29.2)	19.1 (12.2 to 27.7)	16.4 (10.0 to 24.6)	10.6 (4.4 to 20.6)
Irritability: Moderate|	40.9 (20.7 to 63.6)	46.4 (36.8 to 56.1)	39.1 (29.9 to 48.9)	30.3 (19.6 to 42.9)
Irritability: Severe|	0.0 (0.0 to 15.4)	6.4 (2.6 to 12.7)	5.5 (2.0 to 11.5)	0.0 (0.0 to 5.4)
Drowsiness: Any|	40.9 (20.7 to 63.6)	45.5 (35.9 to 55.2)	42.7 (33.3 to 52.5)	25.8 (15.8 to 38.0)
Drowsiness: Mild|	31.8 (13.9 to 54.9)	28.2 (20.0 to 37.6)	24.5 (16.8 to 33.7)	16.7 (8.6 to 27.9)
Drowsiness: Moderate|	9.1 (1.1 to 29.2)	11.8 (6.4 to 19.4)	15.5 (9.3 to 23.6)	7.6 (2.5 to 16.8)
Drowsiness: Severe|	0.0 (0.0 to 15.4)	5.5 (2.0 to 11.5)	2.7 (0.6 to 7.8)	1.5 (0.0 to 8.2)
Loss of or decrease appetite: Any|	36.4 (17.2 to 59.3)	44.5 (35.1 to 54.3)	46.4 (36.8 to 56.1)	34.8 (23.5 to 47.6)
Loss of or decrease appetite: Mild|	18.2 (5.2 to 40.3)	16.4 (10.0 to 24.6)	24.5 (16.8 to 33.7)	13.6 (6.4 to 24.3)
Loss of or decrease appetite: Moderate|	9.1 (1.1 to 29.2)	25.5 (17.6 to 34.6)	14.5 (8.5 to 22.5)	18.2 (9.8 to 29.6)
Loss of or decrease appetite: Severe|	9.1 (1.1 to 29.2)	2.7 (0.6 to 7.8)	7.3 (3.2 to 13.8)	3.0 (0.4 to 10.5)
Antipyretic medication use|	59.1 (36.4 to 79.3)	52.7 (43.0 to 62.3)	40.9 (31.6 to 50.7)	24.2 (14.5 to 36.4)

Notes:

[37] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[38] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[39] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[40] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	66[41]			
Units: percentage of subjects				
number (confidence interval 95%)				

Fever >=38 degrees C|	1.5 (0.0 to 8.2)			
Fever 38 to <38.5 degrees C|	1.5 (0.0 to 8.2)			
Fever 38.5 to <39 degrees C|	0.0 (0.0 to 5.4)			
Fever 39 to <39.5 degrees C|	0.0 (0.0 to 5.4)			
Fever 39.5 to <=40 degrees C|	0.0 (0.0 to 5.4)			
Fever >40 degrees C|	0.0 (0.0 to 5.4)			
Irritability: Any|	33.3 (22.2 to 46.0)			
Irritability: Mild|	13.6 (6.4 to 24.3)			
Irritability: Moderate|	16.7 (8.6 to 27.9)			
Irritability: Severe|	3.0 (0.4 to 10.5)			
Drowsiness: Any|	10.6 (4.4 to 20.6)			
Drowsiness: Mild|	6.1 (1.7 to 14.8)			
Drowsiness: Moderate|	4.5 (0.9 to 12.7)			
Drowsiness: Severe|	0.0 (0.0 to 15.4)			
Loss of or decrease appetite: Any|	10.6 (4.4 to 20.6)			
Loss of or decrease appetite: Mild|	7.6 (2.5 to 16.8)			
Loss of or decrease appetite: Moderate|	1.5 (0.0 to 8.2)			
Loss of or decrease appetite: Severe|	1.5 (0.0 to 8.2)			
Antipyretic medication use|	15.2 (7.5 to 26.1)			

Notes:

[41] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 2

End point title	Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 2[42]

End point description:

Systemic reactions included fever, irritability, drowsiness, loss of or decreased appetite and recorded by using an e-diary. Fever was graded as 38.0 to 38.4 degree C, 38.5 to 38.9 degree C, 39.0 to 39.4 degree C, >39.5 to 40.0 degree C and >40.0 degree C. Irritability was graded as mild (easily consolable), moderate (requiring increased attention) and severe (inconsolable). Drowsiness was graded as mild (Increased or prolonged sleeping bouts), moderate (slightly subdued interfering with daily activity) and severe (disabling not interested in usual daily activity). Loss of or decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Safety population: all subjects who received at least 1 dose of an investigational product (rLP2086 or HAV vaccine) and had safety data available. Here, N signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

within 7 Days after Vaccination 2

Notes:

[42] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44[43]	212[44]	128[45]	22[46]
Units: percentage of subejcts				
number (confidence interval 95%)				
Fever >=38 degrees C|	11.4 (3.8 to 24.6)	14.2 (9.8 to 19.6)	4.7 (1.7 to 9.9)	13.6 (2.9 to 34.9)
Fever 38 to <38.5 degrees C|	6.8 (1.4 to 18.7)	6.6 (3.7 to 10.8)	3.9 (1.3 to 8.9)	13.6 (2.9 to 34.9)
Fever 38.5 to <39 degrees C|	2.3 (0.1 to 12.0)	4.7 (2.3 to 8.5)	0.8 (0.0 to 4.3)	0.0 (0.0 to 15.4)
Fever 39 to <39.5 degrees C|	0.0 (0.0 to 8.0)	1.9 (0.5 to 4.8)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Fever 39.5 to <=40 degrees C|	2.3 (0.1 to 12.0)	0.9 (0.1 to 3.4)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Fever >40 degrees C|	0.0 (0.0 to 8.0)	0.0 (0.0 to 1.7)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Irritability: Any|	45.5 (30.4 to 61.2)	54.7 (47.8 to 61.5)	25.0 (17.8 to 33.4)	50.0 (28.2 to 71.8)
Irritability: Mild|	29.5 (16.8 to 45.2)	18.9 (13.8 to 24.8)	7.0 (3.3 to 12.9)	40.9 (20.7 to 63.6)
Irritability: Moderate|	13.6 (5.2 to 27.4)	33.0 (26.7 to 39.8)	15.6 (9.8 to 23.1)	4.5 (0.1 to 22.8)
Irritability: Severe|	2.3 (0.1 to 12.0)	2.8 (1.0 to 6.1)	2.3 (0.5 to 6.7)	4.5 (0.1 to 22.8)
Drowsiness: Any|	15.9 (6.6 to 30.1)	30.7 (24.5 to 37.3)	11.7 (6.7 to 18.6)	13.6 (2.9 to 34.9)
Drowsiness: Mild|	13.6 (5.2 to 27.4)	18.4 (13.4 to 24.3)	7.0 (3.3 to 12.9)	9.1 (1.1 to 29.2)
Drowsiness: Moderate|	2.3 (0.1 to 12.0)	10.8 (7.0 to 15.8)	3.9 (1.3 to 8.9)	4.5 (0.1 to 22.8)
Drowsiness: Severe|	0.0 (0.0 to 8.0)	1.4 (0.3 to 4.1)	0.8 (0.0 to 4.3)	0.0 (0.0 to 15.4)
Loss of or decreased appetite: Any|	25.0 (13.2 to 40.3)	36.3 (29.8 to 43.2)	18.0 (11.7 to 25.7)	31.8 (13.9 to 54.9)
Loss of or decreased appetite: Mild|	22.7 (11.5 to 37.8)	19.3 (14.3 to 25.3)	9.4 (4.9 to 15.8)	27.3 (10.7 to 50.2)
Loss of or decreased appetite: Moderate|	2.3 (0.1 to 12.0)	12.3 (8.2 to 17.5)	7.8 (3.8 to 13.9)	4.5 (0.1 to 22.8)
Loss of or decreased appetite: Severe|	0.0 (0.0 to 8.0)	4.7 (2.3 to 8.5)	0.8 (0.0 to 4.3)	0.0 (0.0 to 15.4)
Antipyretic medication use|	36.4 (22.4 to 52.2)	33.5 (27.2 to 40.3)	14.8 (9.2 to 22.2)	45.5 (24.4 to 67.8)

Notes:

[43] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[44] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[45] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[46] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety

population)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[47]	105[48]	107[49]	63[50]
Units: percentage of subejcts				
number (confidence interval 95%)				
Fever >=38 degrees C|	9.1 (1.1 to 29.2)	14.3 (8.2 to 22.5)	14.0 (8.1 to 22.1)	6.3 (1.8 to 15.5)
Fever 38 to <38.5 degrees C|	0.0 (0.0 to 15.4)	4.8 (1.6 to 10.8)	8.4 (3.9 to 15.4)	4.8 (1.0 to 13.3)
Fever 38.5 to <39 degrees C|	4.5 (0.1 to 22.8)	6.7 (2.7 to 13.3)	2.8 (0.6 to 8.0)	1.6 (0.0 to 8.5)
Fever 39 to <39.5 degrees C|	0.0 (0.0 to 15.4)	1.9 (0.2 to 6.7)	1.9 (0.2 to 6.6)	0.0 (0.0 to 5.7)
Fever 39.5 to <=40 degrees C|	4.5 (0.1 to 22.8)	1.0 (0.0 to 5.2)	0.9 (0.0 to 5.1)	0.0 (0.0 to 5.7)
Fever >40 degrees C|	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.5)	0.0 (0.0 to 3.4)	0.0 (0.0 to 5.7)
Irritability: Any|	40.9 (20.7 to 63.6)	54.3 (44.3 to 64.0)	55.1 (45.2 to 64.8)	31.7 (20.6 to 44.7)
Irritability: Mild|	18.2 (5.2 to 40.3)	19.0 (12.0 to 27.9)	18.7 (11.8 to 27.4)	7.9 (2.6 to 17.6)
Irritability: Moderate|	22.7 (7.8 to 45.4)	31.4 (22.7 to 41.2)	34.6 (25.6 to 44.4)	22.2 (12.7 to 34.5)
Irritability: Severe|	0.0 (0.0 to 15.4)	3.8 (1.0 to 9.5)	1.9 (0.2 to 6.6)	1.6 (0.0 to 8.5)
Drowsiness: Any|	18.2 (5.2 to 40.3)	37.1 (27.9 to 47.1)	24.3 (16.5 to 33.5)	19.0 (10.2 to 30.9)
Drowsiness: Mild|	18.2 (5.2 to 40.3)	22.9 (15.2 to 32.1)	14.0 (8.1 to 22.1)	9.5 (3.6 to 19.6)
Drowsiness: Moderate|	0.0 (0.0 to 15.4)	13.3 (7.5 to 21.4)	8.4 (3.9 to 15.4)	7.9 (2.6 to 17.6)
Drowsiness: Severe|	0.0 (0.0 to 15.4)	1.0 (0.0 to 5.2)	1.9 (0.2 to 6.6)	1.6 (0.0 to 8.5)
Loss of or decreased appetite: Any|	18.2 (5.2 to 40.3)	41.0 (31.5 to 51.0)	31.8 (23.1 to 41.5)	22.2 (12.7 to 34.5)
Loss of or decreased appetite: Mild|	18.2 (5.2 to 40.3)	19.0 (12.0 to 27.9)	19.6 (12.6 to 28.4)	11.1 (4.6 to 21.6)
Loss of or decreased appetite: Moderate|	0.0 (0.0 to 15.4)	17.1 (10.5 to 25.7)	7.5 (3.3 to 14.2)	9.5 (3.6 to 19.6)
Loss of or decreased appetite: Severe|	0.0 (0.0 to 15.4)	4.8 (1.6 to 10.8)	4.7 (1.5 to 10.6)	1.6 (0.0 to 8.5)
Antipyretic medication use|	27.3 (10.7 to 50.2)	35.2 (26.2 to 45.2)	31.8 (23.1 to 41.5)	19.0 (10.2 to 30.9)

Notes:

[47] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

[48] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

[49] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

[50] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	65[51]			
Units: percentage of subejcts				
number (confidence interval 95%)				
Fever >=38 degrees C|	3.1 (0.4 to 10.7)			
Fever 38 to <38.5 degrees C|	3.1 (0.4 to 10.7)			
Fever 38.5 to <39 degrees C|	0.0 (0.0 to 5.5)			
Fever 39 to <39.5 degrees C|	0.0 (0.0 to 5.5)			
Fever 39.5 to <=40 degrees C|	0.0 (0.0 to 5.5)			
Fever >40 degrees C|	0.0 (0.0 to 5.5)			
Irritability: Any|	18.5 (9.9 to 30.0)			
Irritability: Mild|	6.2 (1.7 to 15.0)			
Irritability: Moderate|	9.2 (3.5 to 19.0)			
Irritability: Severe|	3.1 (0.4 to 10.7)			
Drowsiness: Any|	4.6 (1.0 to 12.9)			
Drowsiness: Mild|	4.6 (1.0 to 12.9)			
Drowsiness: Moderate|	0.0 (0.0 to 5.5)			
Drowsiness: Severe|	0.0 (0.0 to 5.5)			
Loss of or decreased appetite: Any|	13.8 (6.5 to 24.7)			
Loss of or decreased appetite: Mild|	7.7 (2.5 to 17.0)			
Loss of or decreased appetite: Moderate|	6.2 (1.7 to 15.0)			
Loss of or decreased appetite: Severe|	0.0 (0.0 to 5.5)			
Antipyretic medication use|	10.8 (4.4 to 20.9)			

Notes:

[51] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 3

End point title	Percentage of Subjects Reporting Systemic Events and Antipyretic Use Within 7 Days After Vaccination 3[52]

End point description:

Systemic reactions included fever, irritability, drowsiness, loss of or decreased appetite and recorded by using an e-diary. Fever was graded as 38.0 to 38.4 degree C, 38.5 to 38.9 degree C, 39.0 to 39.4 degree C, >39.5 to 40.0 degree C and >40.0 degree C. Irritability was graded as mild (easily consolable), moderate (requiring increased attention) and severe (inconsolable). Drowsiness was graded as mild (Increased or prolonged sleeping bouts), moderate (slightly subdued interfering with daily activity) and severe (disabling not interested in usual daily activity). Loss of or decreased appetite was

graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Safety population: all subjects who received at least 1 dose of an investigational product (rLP2086 or HAV vaccine) and had safety data available. Here, N signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

within 7 Days after Vaccination 3

Notes:

[52] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44[53]	212[54]	128[55]	22[56]
Units: percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C|	4.5 (0.6 to 15.5)	12.7 (8.6 to 18.0)	6.3 (2.7 to 11.9)	4.5 (0.1 to 22.8)
Fever 38 to <38.5 degrees C|	4.5 (0.6 to 15.5)	6.6 (3.7 to 10.8)	3.9 (1.3 to 8.9)	4.5 (0.1 to 22.8)
Fever 38.5 to <39 degrees C|	0.0 (0.0 to 8.0)	2.4 (0.8 to 5.4)	1.6 (0.2 to 5.5)	0.0 (0.0 to 15.4)
Fever 39 to <39.5 degrees C|	0.0 (0.0 to 8.0)	2.4 (0.8 to 5.4)	0.8 (0.0 to 4.3)	0.0 (0.0 to 15.4)
Fever 39.5 to <=40 degrees C|	0.0 (0.0 to 8.0)	1.4 (0.3 to 4.1)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Fever >40 degrees C|	0.0 (0.0 to 8.0)	0.0 (0.0 to 1.7)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
Irritability: Any|	36.4 (22.4 to 52.2)	50.5 (43.5 to 57.4)	27.3 (19.8 to 35.9)	36.4 (17.2 to 59.3)
Irritability: Mild|	20.5 (9.8 to 35.3)	23.6 (18.0 to 29.9)	12.5 (7.3 to 19.5)	22.7 (7.8 to 45.4)
Irritability: Moderate|	15.9 (6.6 to 30.1)	25.0 (19.3 to 31.4)	13.3 (7.9 to 20.4)	13.6 (2.9 to 34.9)
Irritability: Severe|	0.0 (0.0 to 8.0)	1.9 (0.5 to 4.8)	1.6 (0.2 to 5.5)	0.0 (0.0 to 15.4)
Drowsiness: Any|	13.6 (5.2 to 27.4)	34.0 (27.6 to 40.8)	13.3 (7.9 to 20.4)	4.5 (0.1 to 22.8)
Drowsiness: Mild|	13.6 (5.2 to 27.4)	23.6 (18.0 to 29.9)	10.2 (5.5 to 16.7)	4.5 (0.1 to 22.8)
Drowsiness: Moderate|	0.0 (0.0 to 8.0)	8.5 (5.1 to 13.1)	2.3 (0.5 to 6.7)	0.0 (0.0 to 15.4)
Drowsiness: Severe|	0.0 (0.0 to 8.0)	1.9 (0.5 to 4.8)	0.8 (0.0 to 4.3)	0.0 (0.0 to 15.4)
Loss of or decreased appetite: Any|	18.2 (8.2 to 32.7)	34.4 (28.1 to 41.2)	18.0 (11.7 to 25.7)	13.6 (2.9 to 34.9)
Loss of or decreased appetite: Mild|	15.9 (6.6 to 30.1)	17.0 (12.2 to 22.7)	12.5 (7.3 to 19.5)	13.6 (2.9 to 34.9)
Loss of or decreased appetite: Moderate|	0.0 (0.0 to 8.0)	14.6 (10.2 to 20.1)	4.7 (1.7 to 9.9)	0.0 (0.0 to 15.4)
Loss of or decreased appetite: Severe|	2.3 (0.1 to 12.0)	2.8 (1.0 to 6.1)	0.8 (0.0 to 4.3)	0.0 (0.0 to 15.4)
Antipyretic medication use|	18.2 (8.2 to 32.7)	34.0 (27.6 to 40.8)	14.8 (9.2 to 22.2)	18.2 (5.2 to 40.3)

Notes:

[53] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[54] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[55] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[56] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[57]	104[58]	108[59]	65[60]
Units: percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C|	4.5 (0.1 to 22.8)	10.6 (5.4 to 18.1)	14.8 (8.7 to 22.9)	4.6 (1.0 to 12.9)
Fever 38 to <38.5 degrees C|	4.5 (0.1 to 22.8)	6.7 (2.7 to 13.4)	6.5 (2.6 to 12.9)	3.1 (0.4 to 10.7)
Fever 38.5 to <39 degrees C|	0.0 (0.0 to 15.4)	2.9 (0.6 to 8.2)	1.9 (0.2 to 6.5)	1.5 (0.0 to 8.3)
Fever 39 to <39.5 degrees C|	0.0 (0.0 to 15.4)	1.0 (0.0 to 5.2)	3.7 (1.0 to 9.2)	0.0 (0.0 to 5.5)
Fever 39.5 to <=40 degrees C|	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.5)	2.8 (0.6 to 7.9)	0.0 (0.0 to 5.5)
Fever >40 degrees C|	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.5)	0.0 (0.0 to 3.4)	0.0 (0.0 to 5.5)
Irritability: Any|	36.4 (17.2 to 59.3)	56.7 (46.7 to 66.4)	44.4 (34.9 to 54.3)	24.6 (14.8 to 36.9)
Irritability: Mild|	18.2 (5.2 to 40.3)	27.9 (19.5 to 37.5)	19.4 (12.5 to 28.2)	9.2 (3.5 to 19.0)
Irritability: Moderate|	18.2 (5.2 to 40.3)	26.0 (17.9 to 35.5)	24.1 (16.4 to 33.3)	13.8 (6.5 to 24.7)
Irritability: Severe|	0.0 (0.0 to 15.4)	2.9 (0.6 to 8.2)	0.9 (0.0 to 5.1)	1.5 (0.0 to 8.3)
Drowsiness: Any|	22.7 (7.8 to 45.4)	37.5 (28.2 to 47.5)	30.6 (22.1 to 40.2)	13.8 (6.5 to 24.7)
Drowsiness: Mild|	22.7 (7.8 to 45.4)	24.0 (16.2 to 33.4)	23.1 (15.6 to 32.2)	10.8 (4.4 to 20.9)
Drowsiness: Moderate|	0.0 (0.0 to 15.4)	10.6 (5.4 to 18.1)	6.5 (2.6 to 12.9)	3.1 (0.4 to 10.7)
Drowsiness: Severe|	0.0 (0.0 to 15.4)	2.9 (0.6 to 8.2)	0.9 (0.0 to 5.1)	0.0 (0.0 to 5.5)
Loss of or decreased appetite: Any|	22.7 (7.8 to 45.4)	33.7 (24.7 to 43.6)	35.2 (26.2 to 45.0)	16.9 (8.8 to 28.3)
Loss of or decreased appetite: Mild|	22.7 (7.8 to 45.4)	15.4 (9.1 to 23.8)	18.5 (11.7 to 27.1)	9.2 (3.5 to 19.0)
Loss of or decreased appetite: Moderate|	0.0 (0.0 to 15.4)	14.4 (8.3 to 22.7)	14.8 (8.7 to 22.9)	7.7 (2.5 to 17.0)
Loss of or decreased appetite: Severe|	0.0 (0.0 to 15.4)	3.8 (1.1 to 9.6)	1.9 (0.2 to 6.5)	0.0 (0.0 to 5.5)
Antipyretic medication use|	18.2 (5.2 to 40.3)	34.6 (25.6 to 44.6)	33.3 (24.6 to 43.1)	13.8 (6.5 to 24.7)

Notes:

[57] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[58] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[59] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[60] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	63[61]			
Units: percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C|	7.9 (2.6 to 17.6)			
Fever 38 to <38.5 degrees C|	4.8 (1.0 to 13.3)			
Fever 38.5 to <39 degrees C|	1.6 (0.0 to 8.5)			
Fever 39 to <39.5 degrees C|	1.6 (0.0 to 8.5)			
Fever 39.5 to <=40 degrees C|	0.0 (0.0 to 5.7)			
Fever >40 degrees C|	0.0 (0.0 to 5.7)			
Irritability: Any|	30.2 (19.2 to 43.0)			
Irritability: Mild|	15.9 (7.9 to 27.3)			
Irritability: Moderate|	12.7 (5.6 to 23.5)			
Irritability: Severe|	1.6 (0.0 to 8.5)			
Drowsiness: Any|	12.7 (5.6 to 23.5)			
Drowsiness: Mild|	1.6 (0.0 to 8.5)			
Drowsiness: Moderate|	1.6 (0.0 to 8.5)			
Drowsiness: Severe|	1.6 (0.0 to 8.5)			
Loss of or decreased appetite: Any|	19.0 (10.2 to 30.9)			
Loss of or decreased appetite: Mild|	15.9 (7.9 to 27.3)			
Loss of or decreased appetite: Moderate|	1.6 (0.0 to 8.5)			
Loss of or decreased appetite: Severe|	1.6 (0.0 to 8.5)			
Antipyretic medication use|	15.9 (7.9 to 27.3)			

Notes:

[61] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE), Newly Diagnosed Chronic Medical Condition (NDCMC) and Immediate Adverse Event (IAE) Within 30 Days After Vaccination 1

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE), Newly Diagnosed Chronic Medical Condition (NDCMC) and Immediate Adverse Event (IAE) Within 30 Days After Vaccination 1[62]

End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-

threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication; important medical event. MAE was defined as a non-serious AE that resulted in an evaluation at a medical facility. An NDCMC was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Immediate AE was defined as AEs occurring within the first 30 minutes after investigational product administration. Safety analysis population.

End point type	Primary

End point timeframe:

within 30 Days after Vaccination 1

Notes:

[62] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44[63]	220[64]	132[65]	22[66]
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	31.8 (18.6 to 47.6)	40.0 (33.5 to 46.8)	30.3 (22.6 to 38.9)	18.2 (5.2 to 40.3)
SAE|	2.3 (0.1 to 12.0)	1.4 (0.3 to 3.9)	1.5 (0.2 to 5.4)	0.0 (0.0 to 15.4)
MAE	11.4 (3.8 to 24.6)	18.6 (13.7 to 24.4)	17.4 (11.4 to 25.0)	9.1 (1.1 to 29.2)
NDCMC	0.0 (0.0 to 8.0)	0.0 (0.0 to 1.7)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
IAE	2.3 (0.1 to 12.0)	0.0 (0.0 to 1.7)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)

Notes:

[63] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[64] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[65] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[66] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[67]	110[68]	110[69]	66[70]
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	45.5 (24.4 to 67.8)	38.2 (29.1 to 47.9)	41.8 (32.5 to 51.6)	33.3 (22.2 to 46.0)
SAE|	4.5 (0.1 to 22.8)	0.9 (0.0 to 5.0)	1.8 (0.2 to 6.4)	1.5 (0.0 to 8.2)
MAE	13.6 (2.9 to 34.9)	18.2 (11.5 to 26.7)	19.1 (12.2 to 27.7)	18.2 (9.8 to 29.6)
NDCMC	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.3)	0.0 (0.0 to 3.3)	0.0 (0.0 to 5.4)
IAE	4.5 (0.1 to 22.8)	0.0 (0.0 to 3.3)	0.0 (0.0 to 3.3)	0.0 (0.0 to 5.4)

Notes:

[67] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[68] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[69] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

[70] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	66[71]			
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	27.3 (17.0 to 39.6)			
SAE|	1.5 (0.0 to 8.2)			
MAE	16.7 (8.6 to 27.9)			
NDCMC	0.0 (0.0 to 5.4)			
IAE	0.0 (0.0 to 5.4)			

Notes:

[71] - N=subjects with 1st dose of vaccine on Month 0 with safety data(Vaccination 1 safety population)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE), Newly Diagnosed Chronic Medical Condition (NDCMC), Immediate Adverse Event (IAE) Within 30 Days After Vaccination 2

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE), Newly Diagnosed Chronic Medical Condition (NDCMC), Immediate Adverse Event (IAE) Within 30 Days After Vaccination 2[72]

End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication; important medical event. MAE was defined as a non-serious AE that resulted in an evaluation at a medical facility. An NDCMC was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Immediate AE was defined as AEs occurring within the first 30 minutes after investigational product administration. Safety analysis population. Here, N signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

within 30 Days after Vaccination 2

Notes:

[72] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44[73]	213[74]	131[75]	22[76]
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	22.7 (11.5 to 37.8)	34.3 (27.9 to 41.1)	28.2 (20.7 to 36.8)	18.2 (5.2 to 40.3)
SAE|	0.0 (0.0 to 8.0)	1.9 (0.5 to 4.7)	0.8 (0.0 to 4.2)	0.0 (0.0 to 15.4)
MAE	11.4 (3.8 to 24.6)	17.4 (12.5 to 23.1)	18.3 (12.1 to 26.0)	13.6 (2.9 to 34.9)
NDCMC	0.0 (0.0 to 8.0)	0.0 (0.0 to 1.7)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
IAE	0.0 (0.0 to 8.0)	0.0 (0.0 to 2.6)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)

Notes:

[73] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[74] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[75] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[76] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[77]	105[78]	108[79]	66[80]
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	27.3 (10.7 to 50.2)	34.3 (25.3 to 44.2)	34.3 (25.4 to 44.0)	24.2 (14.5 to 36.4)
SAE|	0.0 (0.0 to 15.4)	3.8 (1.0 to 9.5)	0.0 (0.0 to 3.4)	1.5 (0.0 to 8.2)
MAE	9.1 (1.1 to 29.2)	16.2 (9.7 to 24.7)	18.5 (11.7 to 27.1)	13.6 (6.4 to 24.3)
NDCMC	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.5)	0.0 (0.0 to 3.4)	0.0 (0.0 to 5.4)
IAE	0.0 (0.0 to 15.4)	0.0 (0.0 to 5.2)	0.0 (0.0 to 3.4)	0.0 (0.0 to 5.4)

Notes:

[77] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[78] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[79] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)
[80] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

End point values	Group 3: HAV/Saline (>=18 months to <24			

	months)			
Subject group type	Subject analysis set			
Number of subjects analysed	65[81]			
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	32.3 (21.2 to 45.1)			
SAE|	0.0 (0.0 to 5.5)			
MAE	23.1 (13.5 to 35.2)			
NDCMC	0.0 (0.0 to 5.5)			
IAE	0.0 (0.0 to 5.4)			

Notes:

[81] - N=subjects with 2nd dose of vaccine on Month 2 with safety data(Vaccination 2 safety population)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE), Newly Diagnosed Chronic Medical Condition (NDCMC), Immediate Adverse Event (IAE) Within 30 Days After Vaccination 3

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE), Newly Diagnosed Chronic Medical Condition (NDCMC), Immediate Adverse Event (IAE) Within 30 Days After Vaccination 3[82]

End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication; important medical event. MAE was defined as a non-serious AE that resulted in an evaluation at a medical facility. An NDCMC was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Immediate AE was defined as AEs occurring within the first 30 minutes after investigational product administration. Safety analysis population. Here, N signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

within 30 Days after Vaccination 3

Notes:

[82] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44[83]	212[84]	129[85]	22[86]
Units: percentage of subjects				
number (confidence interval 95%)				

AE|	29.5 (16.8 to 45.2)	27.8 (21.9 to 34.4)	26.4 (19.0 to 34.8)	18.2 (5.2 to 40.3)
SAE|	0.0 (0.0 to 8.0)	0.5 (0.0 to 2.6)	0.8 (0.0 to 4.2)	0.0 (0.0 to 15.4)
MAE	18.2 (8.2 to 32.7)	15.1 (10.6 to 20.6)	16.3 (10.4 to 23.8)	9.1 (1.1 to 29.2)
NDCMC	0.0 (0.0 to 8.0)	0.0 (0.0 to 1.7)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)
IAE	0.0 (0.0 to 8.0)	0.0 (0.0 to 2.6)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)

Notes:

[83] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[84] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[85] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[86] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[87]	104[88]	108[89]	65[90]
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	40.9 (20.7 to 63.6)	25.0 (17.0 to 34.4)	30.6 (22.1 to 40.2)	24.6 (14.8 to 36.9)
SAE|	0.0 (0.0 to 15.4)	1.0 (0.0 to 5.2)	0.0 (0.0 to 3.4)	1.5 (0.0 to 8.3)
MAE	27.3 (10.7 to 50.2)	13.5 (7.6 to 21.6)	16.7 (10.2 to 25.1)	12.3 (5.5 to 22.8)
NDCMC	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.5)	0.0 (0.0 to 3.4)	0.0 (0.0 to 5.5)
IAE	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.5)	0.0 (0.0 to 5.1)	0.0 (0.0 to 5.5)

Notes:

[87] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[88] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[89] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

[90] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	64[91]			
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	28.1 (17.6 to 40.8)			
SAE|	0.0 (0.0 to 5.6)			
MAE	20.3 (11.3 to 32.2)			
NDCMC	0.0 (0.0 to 5.6)			
IAE	0.0 (0.0 to 5.6)			

Notes:

[91] - N=subjects with 3rd dose of vaccine on Month 6 with safety data(Vaccination 3 safety population)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE) and Newly Diagnosed Chronic Medical Condition (NDCMC) Within 30 Days After Any Vaccination

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE) and Newly Diagnosed Chronic Medical Condition (NDCMC) Within 30 Days After Any Vaccination[92]

End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication; important medical event. A MAE was defined as a non-serious AE that resulted in an evaluation at a medical facility. An NDCMC was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Safety population: all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

within 30 Days after any Vaccination

Notes:

[92] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44	220	132	22
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	50.0 (34.6 to 65.4)	58.2 (51.4 to 64.8)	53.8 (44.9 to 62.5)	36.4 (17.2 to 59.3)
SAE|	2.3 (0.1 to 12.0)	3.6 (1.6 to 7.0)	3.0 (0.8 to 7.6)	0.0 (0.0 to 15.4)
MAE	31.8 (18.6 to 47.6)	36.4 (30.0 to 43.1)	35.6 (27.5 to 44.4)	22.7 (7.8 to 45.4)
NDCMC	0.0 (0.0 to 8.0)	0.0 (0.0 to 1.7)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)

End point values	Group 1: 60-µg bivalent	Group 2: 120-µg bivalent	Group 2: 120-µg bivalent	Group 3: HAV/Saline

	rLP2086 (>=18 months to <24 months)	rLP2086 (>=12 months to <18 months)	rLP2086 (>=18 months to <24 months)	(>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	110	110	66
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	63.6 (40.7 to 82.8)	54.5 (44.8 to 64.1)	61.8 (52.1 to 70.9)	53.0 (40.3 to 65.4)
SAE|	4.5 (0.1 to 22.8)	5.5 (2.0 to 11.5)	1.8 (0.2 to 6.4)	4.5 (0.9 to 12.7)
MAE	40.9 (20.7 to 63.6)	32.7 (24.1 to 42.3)	40.0 (30.8 to 49.8)	31.8 (20.9 to 44.4)
NDCMC	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.3)	0.0 (0.0 to 3.3)	0.0 (0.0 to 5.4)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	66			
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	54.5 (41.8 to 66.9)			
SAE|	1.5 (0.0 to 8.2)			
MAE	39.4 (27.6 to 52.2)			
NDCMC	0.0 (0.0 to 5.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE) and Newly Diagnosed Chronic Medical Condition (NDCMC) During the Vaccination Phase

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE), Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE) and Newly Diagnosed Chronic Medical Condition (NDCMC) During the Vaccination Phase[93]

End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication; important medical event. A MAE was defined as a non-serious AE that resulted in an evaluation at a medical facility. An NDCMC was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Safety population: all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

From the Vaccination 1 up to 1 month after Vaccination 3

Notes:

[93] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44	220	132	22
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	65.9 (50.1 to 79.5)	70.0 (63.5 to 76.0)	64.4 (55.6 to 72.5)	54.5 (32.2 to 75.6)
SAE|	4.5 (0.6 to 15.5)	7.3 (4.2 to 11.5)	5.3 (2.2 to 10.6)	0.0 (0.0 to 15.4)
MAE	40.9 (26.3 to 56.8)	50.9 (44.1 to 57.7)	43.2 (34.6 to 52.1)	36.4 (17.2 to 59.3)
NDCMC	0.0 (0.0 to 8.0)	0.5 (0.0 to 2.5)	0.0 (0.0 to 2.8)	0.0 (0.0 to 15.4)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	110	110	66
Units: percentage of subjects				
number (confidence interval 95%)				
AE|	77.3 (54.6 to 92.2)	68.2 (58.6 to 76.7)	71.8 (62.4 to 80.0)	65.2 (52.4 to 76.5)
SAE|	9.1 (1.1 to 29.2)	10.9 (5.8 to 18.3)	3.6 (1.0 to 9.0)	4.5 (0.9 to 12.7)
MAE	45.5 (24.4 to 67.8)	47.3 (37.7 to 57.0)	54.5 (44.8 to 64.1)	42.4 (30.3 to 55.2)
NDCMC	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.3)	0.0 (0.0 to 5.0)	0.0 (0.0 to 5.4)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	66			
Units: percentage of subjects				
number (confidence interval 95%)				

AE|	63.6 (50.9 to 75.1)			
SAE|	6.1 (1.7 to 14.8)			
MAE	43.9 (31.7 to 56.7)			
NDCMC	0.0 (0.0 to 5.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE) and Newly Diagnosed Chronic Medical Condition (NDCMC) During the Follow up Phase

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE) and Newly Diagnosed Chronic Medical Condition (NDCMC) During the Follow up Phase[94]

End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly; lack of efficacy in an approved indication; important medical event. A MAE was defined as a non-serious AE that resulted in an evaluation at a medical facility. An NDCMC was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Safety population: all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available. Here, N signifies number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

From 1 month after Vaccination 3 (Visit 7) up to 6 months after Vaccination 3 (Visit 8)

Notes:

[94] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44[95]	215[96]	128[97]	22[98]
Units: percentage of subjects				
number (confidence interval 95%)				
SAE	6.8 (1.4 to 18.7)	2.3 (0.8 to 5.3)	1.6 (0.2 to 5.5)	4.5 (0.1 to 22.8)
MAE	31.8 (18.6 to 47.6)	31.2 (25.0 to 37.8)	29.7 (21.9 to 38.4)	22.7 (7.8 to 45.4)
NDCMC	2.3 (0.1 to 12.0)	0.0 (0.0 to 1.7)	0.0 (0.0 to 2.8)	4.5 (0.1 to 22.8)

Notes:

[95] - N=all treated subjects with safety data available from visit 7 to visit 8 (follow up safety set)

[96] - N=all treated subjects with safety data available from visit 7 to visit 8 (follow up safety set)

[97] - N=all treated subjects with safety data available from visit 7 to visit 8 (follow up safety set)

[98] - N=all treated subjects with safety data available from visit 7 to visit 8 (follow up safety set)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22[99]	108[100]	107[101]	65[102]
Units: percentage of subjects				
number (confidence interval 95%)				
SAE	9.1 (1.1 to 29.2)	0.9 (0.0 to 5.1)	3.7 (1.0 to 9.3)	1.5 (0.0 to 8.3)
MAE	40.9 (20.7 to 63.6)	29.6 (21.2 to 39.2)	32.7 (24.0 to 42.5)	30.8 (19.9 to 43.4)
NDCMC	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.4)	0.0 (0.0 to 3.4)	0.0 (0.0 to 5.5)

Notes:

[99] - N=all treated subjects with safety data available from visit 7 to visit 8 (follow up safety set)

[100] - N=all treated subjects with safety data available from visit 7 to visit 8 (follow up safety set)

[101] - N=all treated subjects with safety data available from visit 7 to visit 8 (follow up safety set)

[102] - N=all treated subjects with safety data available from visit 7 to visit 8 (follow up safety set)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	63[103]			
Units: percentage of subjects				
number (confidence interval 95%)				
SAE	1.6 (0.0 to 8.5)			
MAE	28.6 (17.9 to 41.3)			
NDCMC	0.0 (0.0 to 5.7)			

Notes:

[103] - N=all treated subjects with safety data available from visit 7 to visit 8 (follow up safety set)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE) and Newly Diagnosed Chronic Medical Condition (NDCMC)Throughout the Study

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE), Medically Attended Adverse Event (MAE) and Newly Diagnosed Chronic Medical Condition (NDCMC)Throughout the Study[104]

End point description:

An AE was any untoward medical occurrence in a subject who received investigational product without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity;

congenital anomaly; lack of efficacy in an approved indication; important medical event. A MAE was defined as a non-serious AE that resulted in an evaluation at a medical facility. An NDCMC was defined as a disease or medical condition that was not identified prior to study start and was expected to be persistent or otherwise long-lasting in its effects. Safety population: all subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/saline) and had safety data available.

End point type	Primary

End point timeframe:

From Vaccination 1 up to 6 months after Vaccination 3

Notes:

[104] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	44	220	132	22
Units: percentage of subjects				
number (confidence interval 95%)				
SAE	9.1 (2.5 to 21.7)	8.6 (5.3 to 13.2)	6.1 (2.7 to 11.6)	4.5 (0.1 to 22.8)
MAE	61.4 (45.5 to 75.6)	58.6 (51.8 to 65.2)	56.1 (42.7 to 64.7)	54.5 (32.2 to 75.6)
NDCMC	2.3 (0.1 to 12.0)	0.5 (0.0 to 2.5)	0.0 (0.0 to 2.8)	4.5 (0.1 to 22.8)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	110	110	66
Units: percentage of subjects				
number (confidence interval 95%)				
SAE	13.6 (2.9 to 34.9)	10.9 (5.8 to 18.3)	6.4 (2.6 to 12.7)	6.1 (1.7 to 14.8)
MAE	68.2 (45.1 to 86.1)	54.5 (44.8 to 64.1)	62.7 (53.0 to 71.8)	59.1 (46.3 to 71.0)
NDCMC	0.0 (0.0 to 15.4)	0.0 (0.0 to 3.3)	0.0 (0.0 to 5.0)	0.0 (0.0 to 5.4)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	66			
Units: percentage of subjects				

number (confidence interval 95%)				
SAE	6.1 (1.7 to 14.8)			
MAE	53.0 (40.3 to 65.4)			
NDCMC	0.0 (0.0 to 5.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titer Between 12 Months to Less Than (<) 24 Months >= LLOQ for Each of the 4 Primary MnB Test Strains 1 Month After Vaccination 3

End point title	Percentage of Subjects With hSBA Titer Between 12 Months to Less Than (<) 24 Months >= LLOQ for Each of the 4 Primary MnB Test Strains 1 Month After Vaccination 3

End point description:

Percentage of subjects achieving hSBA titer >= LLOQ were computed along with corresponding 2-sided 95% CIs. LLOQ was 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44). Evaluable immunogenicity population: all eligible subjects randomized to study received,scheduled investigational products, had pre and post vaccination blood drawn with valid and determinate assay results and had no important protocol deviation. Here, N signifies number of subjects evaluable for this endpoint and n signifies number of subjects analyzed at specific time points only.

End point type	Secondary

End point timeframe:

1 Month After Vaccination 3

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	96	60	
Units: percentage of subjects				
number (confidence interval 95%)				
PMB80 (A22)| (n =20, 96, 60)	90.0 (68.3 to 98.8)	89.6 (81.7 to 94.9)	5.0 (1.0 to 13.9)	
PMB2001 (A56)| (n =19, 95, 54)	100.0 (82.4 to 100.0)	100.0 (96.2 to 100.0)	1.9 (0.0 to 9.9)	
PMB2948 (B24)| (n =20, 95, 60)	85.0 (62.1 to 96.8)	71.6 (61.4 to 80.4)	5.0 (1.0 to 13.9)	
PMB2707 (B44)| (n =19, 94, 54)	89.5 (66.9 to 98.7)	86.2 (77.5 to 92.4)	0.0 (0.0 to 6.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titer >= LLOQ for Each of the 4 Primary MnB Test Strains 1 Month After Vaccination 2

End point title	Percentage of Subjects With hSBA Titer >= LLOQ for Each of the 4 Primary MnB Test Strains 1 Month After Vaccination 2

End point description:

Percentage of subjects achieving hSBA titer >= LLOQ were computed along with corresponding 2-sided 95% CIs. LLOQ was 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44). Evaluable immunogenicity population: all eligible subjects randomized to study received,scheduled investigational products, had pre and post vaccination blood drawn with valid and determinate assay results and had no important protocol deviation. Here, N signifies number of subjects evaluable for this endpoint and n signifies number of subjects analyzed at specific time points only.

End point type	Secondary

End point timeframe:

1 month (Mon) after Vaccination (Vac) 2

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	95	59	10
Units: percentage of subjects				
number (confidence interval 95%)				
PMB80[A22]| (n=10,9,19,45,50,95,30,29,59)	78.9 (54.4 to 93.9)	74.7 (64.8 to 83.1)	1.7 (0.0 to 9.1)	90.0 (55.5 to 99.7)
PMB2001[A56]| (n=9,10,19,47,48,95,23,29,52)	94.7 (74.0 to 99.9)	100.0 (96.2 to 100.0)	0.0 (0.0 to 6.8)	100.0 (66.4 to 100.0)
PMB2948[B24]| (n=10,9,19, 42,44,86,30,29, 59)	57.9 (33.5 to 79.7)	33.7 (23.9 to 44.7)	1.7 (0.0 to 9.1)	70.0 (34.8 to 93.3)
PMB2707[B44]| (n =9,10,19,47,47,94,23,29,52)	68.4 (43.4 to 87.4)	68.1 (57.7 to 77.3)	0.0 (0.0 to 6.8)	77.8 (40.0 to 97.2)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	47	50	30
Units: percentage of subjects				
number (confidence interval 95%)				
PMB80[A22]| (n=10,9,19,45,50,95,30,29,59)	66.7 (29.9 to 92.5)	64.4 (48.8 to 78.1)	84.0 (70.9 to 92.8)	0.0 (0.0 to 11.6)
PMB2001[A56]| (n=9,10,19,47,48,95,23,29,52)	90.0 (55.5 to 99.7)	100.0 (92.5 to 100.0)	100.0 (92.6 to 100.0)	0.0 (0.0 to 14.8)
PMB2948[B24]| (n=10,9,19, 42,44,86,30,29, 59)	44.4 (13.7 to 78.8)	23.8 (12.1 to 39.5)	43.2 (28.3 to 59.0)	0.0 (0.0 to 11.6)
PMB2707[B44]| (n =9,10,19,47,47,94,23,29,52)	60.0 (26.2 to 87.8)	72.3 (57.4 to 84.4)	63.8 (48.5 to 77.3)	0.0 (0.0 to 14.8)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: percentage of subjects				
number (confidence interval 95%)				
PMB80[A22]| (n=10,9,19,45,50,95,30,29,59)	3.4 (0.1 to 17.8)			
PMB2001[A56]| (n=9,10,19,47,48,95,23,29,52)	0.0 (0.0 to 11.9)			
PMB2948[B24]| (n=10,9,19, 42,44,86,30,29, 59)	3.4 (0.1 to 17.8)			
PMB2707[B44]| (n =9,10,19,47,47,94,23,29,52)	0.0 (0.0 to 11.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Serum Bactericidal Assay Using hSBA Titers >=1:4, >=1:8, >=1:16, >=1:32, >=1:64 and >=1:128 for Each of the 4 Primary Test Strains

End point title	Percentage of Subjects With Serum Bactericidal Assay Using hSBA Titers >=1:4, >=1:8, >=1:16, >=1:32, >=1:64 and >=1:128 for Each of the 4 Primary Test Strains

End point description:

Percentage of subjects achieving hSBA titer >= LLOQ were computed along with corresponding 2-sided 95% CIs. LLOQ was 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44). Evaluable immunogenicity population: all eligible subjects randomized to study received,scheduled investigational products, had pre and post vaccination blood drawn with valid and determinate assay results and had no important protocol deviation. Here, N signifies number of subjects evaluable for this endpoint and n signifies number of subjects analyzed at specific time points only.

End point type	Secondary

End point timeframe:

Before Vaccination 1 (T1), 1 month after Vaccination 2 (T2), 1 month after Vaccination 3 (T3)

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	21	97	61	10
Units: percentage of subjects				
number (confidence interval 95%)				

T1:PMB80[A22]-1:4(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 16.8)	4.1 (1.1 to 10.2)	1.6 (0.0 to 8.8)	0.0 (0.0 to 33.6)
T1:PMB80[A22]-1:8(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 16.8)	3.1 (0.6 to 8.8)	1.6 (0.0 to 8.8)	0.0 (0.0 to 33.6)
T1:PMB80[A22]-1:16(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 16.8)	3.1 (0.6 to 8.8)	1.6 (0.0 to 8.8)	0.0 (0.0 to 33.6)
T1:PMB80[A22]-1:32(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 16.8)	2.1 (0.3 to 7.3)	0.0 (0.0 to 5.9)	0.0 (0.0 to 33.6)
T1:PMB80[A22]-1:64(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 16.8)	1.0 (0.0 to 5.6)	0.0 (0.0 to 5.9)	0.0 (0.0 to 33.6)
T1:PMB80[A22]-1:128(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 16.8)	1.0 (0.0 to 5.6)	0.0 (0.0 to 5.9)	0.0 (0.0 to 33.6)
T1:PMB2001(A56)-1:4(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 17.6)	2.1 (0.3 to 7.4)	1.9 (0.0 to 10.1)	0.0 (0.0 to 33.6)
T1:PMB2001(A56)-1:8(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 17.6)	1.1 (0.0 to 5.7)	0.0 (0.0 to 6.7)	0.0 (0.0 to 33.6)
T1:PMB2001(A56)-1:16(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 17.6)	1.1 (0.0 to 5.7)	0.0 (0.0 to 6.7)	0.0 (0.0 to 33.6)
T1:PMB2001(A56)-1:32(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 17.6)	1.1 (0.0 to 5.7)	0.0 (0.0 to 6.7)	0.0 (0.0 to 33.6)
T1:PMB2001(A56)-1:64(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 17.6)	0.0 (0.0 to 3.8)	0.0 (0.0 to 6.7)	0.0 (0.0 to 33.6)
T1:PMB2001(A56)-1:128,n=9,10,19,46,49,95,24,29,53	0.0 (0.0 to 17.6)	0.0 (0.0 to 3.8)	0.0 (0.0 to 6.7)	0.0 (0.0 to 33.6)
T1:PMB2948(B24)-1:4(n=10,11,21,46,51,97,31,30,61)	4.8 (0.1 to 23.8)	2.1 (0.3 to 7.3)	1.6 (0.0 to 8.8)	0.0 (0.0 to 30.8)
T1:PMB2948(B24)-1:8(n=10,11,21,46,51,97,31,30,61)	4.8 (0.1 to 23.8)	2.1 (0.3 to 7.3)	1.6 (0.0 to 8.8)	0.0 (0.0 to 30.8)
T1:PMB2948(B24)-1:16,n=10,11,21,46,51,97,31,30,61	4.8 (0.1 to 23.8)	2.1 (0.3 to 7.3)	1.6 (0.0 to 8.8)	0.0 (0.0 to 30.8)
T1:PMB2948(B24)-1:32,n=10,11,21,46,51,97,31,30,61	4.8 (0.1 to 23.8)	0.0 (0.0 to 3.7)	1.6 (0.0 to 8.8)	0.0 (0.0 to 30.8)
T1:PMB2948(B24)-1:64,n=10,11,21,46,51,97,31,30,61	0.0 (0.0 to 16.1)	0.0 (0.0 to 3.7)	1.6 (0.0 to 8.8)	0.0 (0.0 to 30.8)
T1:PMB2948(B24)-1:128n=10,11,21,46,51,97,31,30,61	0.0 (0.0 to 16.1)	0.0 (0.0 to 3.7)	0.0 (0.0 to 5.9)	0.0 (0.0 to 30.8)
T1:PMB2707(B44)-1:4(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 17.6)	1.1 (0.0 to 5.7)	0.0 (0.0 to 6.6)	0.0 (0.0 to 33.6)
T1:PB2707(B44)-1:8(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 17.6)	1.1 (0.0 to 5.7)	0.0 (0.0 to 6.6)	0.0 (0.0 to 33.6)
T1:PMB2707(B44)-1:16(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 17.6)	0.0 (0.0 to 3.8)	0.0 (0.0 to 6.6)	0.0 (0.0 to 33.6)
T1:PMB2707(B44)-1:32(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 17.6)	0.0 (0.0 to 3.8)	0.0 (0.0 to 6.6)	0.0 (0.0 to 33.6)
T1:PMB2707(B44)-1:64(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 17.6)	0.0 (0.0 to 3.8)	0.0 (0.0 to 6.6)	0.0 (0.0 to 33.6)
T1:PMB2707(B44)-1:128,n=9,10,19,46,49,95,24,30,54	0.0 (0.0 to 17.6)	0.0 (0.0 to 3.8)	0.0 (0.0 to 6.6)	0.0 (0.0 to 33.6)
T2:PMB80[A22]-1:4(n=10,9,19,45,50,95,30,29,59)	78.9 (54.4 to 93.9)	75.8 (65.9 to 84.0)	1.7 (0.0 to 9.1)	90.0 (55.5 to 99.7)
T2:PMB80[A22]-1:8(n=10,9,19,45,50,95,30,29,59)	78.9 (54.4 to 93.9)	75.8 (65.9 to 84.0)	1.7 (0.0 to 9.1)	90.0 (55.5 to 99.7)
T2:PMB80[A22]-1:32(n=10,9,19,45,50,95,30,29,59)	63.2 (38.4 to 83.7)	58.9 (48.4 to 68.9)	1.7 (0.0 to 9.1)	80.0 (44.5 to 97.5)
T2:PMB80[A22]-1:64(n=10,9,19,45,50,95,30,29,59)	36.8 (16.3 to 61.6)	34.7 (25.3 to 45.2)	1.7 (0.0 to 9.1)	50.0 (18.7 to 81.3)
T2:PMB80[A22]-1:128(n=10,9,19,45,50,95,30,29,59)	21.1 (6.1 to 45.6)	13.7 (7.5 to 22.3)	1.7 (0.0 to 9.1)	20.0 (2.5 to 55.6)
T2:PMB200[A56]-1:4(n=9,10,19,47,48,95,23,29,52)	100.0 (82.4 to 100.0)	100.0 (96.2 to 100.0)	1.9 (0.0 to 10.3)	100.0 (66.4 to 100.0)
T2:PMB2001[A56]-1:16(n=9,10,19,47,48,95,23,29,52)	94.7 (74.0 to 99.9)	100.0 (96.2 to 100.0)	0.0 (0.0 to 6.8)	100.0 (66.4 to 100.0)

T2:PMB2001[A56]-1:32(n =9,10,19,47,48,95,23,29,52)	94.7 (74.0 to 99.9)	95.8 (89.6 to 98.8)	0.0 (0.0 to 6.8)	100.0 (66.4 to 100.0)
T2:PMB2001[A56]-1:64(n =9,10,19,47,48,95,23,29,52)	84.2 (60.4 to 96.6)	86.3 (77.7 to 92.5)	0.0 (0.0 to 6.8)	100.0 (66.4 to 100.0)
T2:PMB2001[A56]-1:128,n=9,10,19,47,48,95,23,29,52	47.4 (24.4 to 71.1)	56.8 (46.3 to 67.0)	0.0 (0.0 to 6.8)	44.4 (13.7 to 78.8)
T2:PMB2948(B24)-1:4(n=10,9,19,42,44,86,30,29,59)	57.9 (33.5 to 79.7)	36.0 (26.0 to 47.1)	1.7 (0.0 to 9.1)	70.0 (34.8 to 93.3)
T2:PMB2948(B24)-1:16(n=10,9,19,42,44,86,30,29,59)	47.4 (24.4 to 71.7)	32.6 (22.8 to 43.5)	1.7 (0.0 to 9.1)	60.0 (26.2 to 87.8)
T2:PMB2948(B24)-1:32(n=10,9,19,42,44,86,30,29,59)	5.3 (0.1 to 26.0)	14.0 (7.4 to 23.1)	1.7 (0.0 to 9.1)	10.0 (0.3 to 44.5)
T2:PMB2948(B24)-1:64(n=10,9,19,42,44,86,30,29,59)	0.0 (0.0 to 17.6)	3.5 (0.7 to 9.9)	0.0 (0.0 to 6.1)	0.0 (0.0 to 30.8)
T2:PMB2948(B24)-1:128,n=10,9,19,42,44,86,30,29,59	0.0 (0.0 to 17.6)	1.2 (0.0 to 6.3)	0.0 (0.0 to 6.1)	0.0 (0.0 to 30.8)
T2:PMB2707(B44)-1:4(n= 9,10,19,47,47,94,23,29,52)	73.7 (48.8 to 90.9)	68.1 (57.7 to 77.3)	0.0 (0.0 to 6.8)	77.8 (40.0 to 97.2)
T2:PMB2707(B44)-1:16(n=9,10,19,47,47,94,23,29,52)	68.4 (43.4 to 87.4)	67.0 (56.6 to 76.4)	0.0 (0.0 to 6.8)	77.8 (40.0 to 97.2)
T2:PMB2707(B44)-1:32(n=9,10,19,47,47,94,23,29,52)	57.9 (33.5 to 79.7)	56.4 (45.8 to 66.6)	0.0 (0.0 to 6.8)	55.6 (21.2 to 86.3)
T2:PMB2707(B44)-1:64(n=9,10,19,47,47,94,23,29,52)	31.6 (12.6 to 56.6)	24.5 (16.2 to 34.4)	0.0 (0.0 to 6.8)	33.3 (7.5 to 70.1)
T2:PMB270(B44)-1:128(n=9,10,19,47,47,94,23,29,52)	10.5 (1.3 to 33.1)	10.6 (5.2 to 18.7)	0.0 (0.0 to 6.8)	11.1 (0.3 to 48.2)
T3:PMB80(A22)-1:4(n=9,11,20,45,51,96,31,29,60)	90.0 (68.3 to 98.8)	89.6 (81.7 to 94.9)	6.7 (1.8 to 16.2)	88.9 (51.8 to 99.7)
T3:PMB80(A22)-1:8(n=9,11,20,45,51,96,31,29,60)	90.0 (68.3 to 98.8)	89.6 (81.7 to 94.9)	6.7 (1.8 to 16.2)	88.9 (51.8 to 99.7)
T3:PMB80(A22)-1:32(n=9,11,20,45,51,96,31,29,60)	85.0 (62.1 to 96.8)	84.4 (75.5 to 91.0)	3.3 (0.4 to 11.5)	88.9 (51.8 to 99.7)
T3:PMB80(A22)-1:64(n=9,11,20,45,51,96,31,29,60)	70.0 (45.7 to 88.1)	66.7 (56.3 to 76.0)	1.7 (0.0 to 8.9)	66.7 (29.9 to 92.5)
T3:PMB80(A22)-1:128(n=9,11,20,45,51,96,31,29,60)	50.0 (27.2 to 72.8)	43.8 (33.6 to 54.3)	0.0 (0.0 to 6.1)	44.4 (13.7 to 78.8)
T3:PMB2001(A56)-1:4(n=9,10,19,47,48,95,24,30,54)	100.0 (82.4 to 100.0)	100.0 (96.2 to 100.0)	9.3 (3.1 to 20.3)	100.0 (66.4 to 100.0)
T3:PMB2001(A56)-1:16(n=9,10,19,47,48,95,24,30,54)	100.0 (82.4 to 100.0)	98.9 (94.3 to 100.0)	1.9 (0.0 to 9.9)	100.0 (66.4 to 100.0)
T3:PMB2001(A56)-1:32(n=9,10,19,47,48,95,24,30,54)	94.7 (74.0 to 99.9)	95.8 (89.6 to 98.8)	1.9 (0.0 to 9.9)	100.0 (66.4 to 100.0)
T3:PMB2001(A56)-1:64(n=9,10,19,47,48,95,24,30,54)	89.5 (66.9 to 98.7)	89.5 (81.5 to 94.8)	0.0 (0.0 to 6.6)	100.0 (66.4 to 100.0)
T3:PMB2001(A56)-1:128,n=9,10,19,47,48,95,24,30,54	68.4 (43.4 to 87.4)	83.2 (74.1 to 90.1)	0.0 (0.0 to 6.6)	55.6 (21.2 to 86.3)
T3:PMB2948(B24)-1:4(n=9,11,20,45,50,95,31,29,60)	85.0 (62.1 to 96.8)	71.6 (61.4 to 80.4)	5.0 (1.0 to 13.9)	88.9 (51.8 to 99.7)
T3:PMB2948(B24)-1:16(n=9,11,20,45,50,95,31,29,60)	75.0 (50.9 to 91.3)	67.4 (57.0 to 76.6)	5.0 (1.0 to 13.9)	88.9 (51.8 to 99.7)
T3:PMB2948(B24)-1:32(n=9,11,20,45,50,95,31,29,60)	40.0 (19.1 to 63.9)	35.8 (26.2 to 46.3)	1.7 (0.0 to 8.9)	44.4 (13.7 to 78.8)
T3:PMB2948(B24)-1:64(n=9,11,20,45,50,95,31,29,60)	15.0 (3.2 to 37.9)	13.7 (7.5 to 22.3)	0.0 (0.0 to 6.0)	11.1 (0.3 to 48.2)
T3:PMB2948(B24)-1:128,n=9,11,20,45,50,95,31,29,60	5.0 (0.1 to 24.9)	2.1 (0.3 to 7.4)	0.0 (0.0 to 6.0)	0.0 (0.0 to 33.6)
T3:PMB2707(B44)-1:4(n=9,10,19,47,47,94,24,30,54)	89.5 (66.9 to 98.7)	87.2 (78.8 to 93.2)	0.0 (0.0 to 6.6)	88.9 (51.8 to 99.7)
T3:PMB2707(B44)-1:16(n=9,10,19,47,47,94,24,30,54)	84.2 (60.4 to 96.6)	86.2 (77.5 to 92.4)	0.0 (0.0 to 6.6)	77.8 (40.0 to 97.2)
T3:PMB2707(B44)-1:32(n=9,10,19,47,47,94,24,30,54)	63.2 (38.4 to 83.7)	76.6 (66.7 to 84.7)	0.0 (0.0 to 6.6)	55.6 (21.2 to 86.3)

T3:PMB2707(B44)-1:64(n=9,10,19,47,47,94,24,30,54	36.8 (16.3 to 61.6)	58.5 (47.9 to 68.6)	0.0 (0.0 to 6.6)	44.4 (13.7 to 78.8)
T3:PMB2707(B44)-1:128,n=9,10,19,47,47,94,24,30,54	21.1 (6.1 to 45.6)	31.9 (22.7 to 42.3)	0.0 (0.0 to 6.6)	22.2 (2.8 to 60.0)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	47	51	31
Units: percentage of subjects				
number (confidence interval 95%)				
T1:PMB80[A22]-1:4(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 28.5)	4.3 (0.5 to 14.8)	3.9 (0.5 to 13.5)	0.0 (0.0 to 11.2)
T1:PMB80[A22]-1:8(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 28.5)	2.2 (0.1 to 11.5)	3.9 (0.5 to 13.5)	0.0 (0.0 to 11.2)
T1:PMB80[A22]-1:16(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 28.5)	2.2 (0.1 to 11.5)	3.9 (0.5 to 13.5)	0.0 (0.0 to 11.2)
T1:PMB80[A22]-1:32(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 28.5)	2.2 (0.1 to 11.5)	2.0 (0.0 to 10.4)	0.0 (0.0 to 11.2)
T1:PMB80[A22]-1:64(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 28.5)	2.2 (0.1 to 11.5)	0.0 (0.0 to 7.0)	0.0 (0.0 to 11.2)
T1:PMB80[A22]-1:128(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 28.5)	2.2 (0.1 to 11.5)	0.0 (0.0 to 7.0)	0.0 (0.0 to 11.2)
T1:PMB2001(A56)-1:4(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 30.8)	0.0 (0.0 to 7.7)	4.1 (0.5 to 14.0)	4.2 (0.1 to 21.1)
T1:PMB2001(A56)-1:8(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 30.8)	0.0 (0.0 to 7.7)	2.0 (0.1 to 10.9)	0.0 (0.0 to 14.2)
T1:PMB2001(A56)-1:16(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 30.8)	0.0 (0.0 to 7.7)	2.0 (0.1 to 10.9)	0.0 (0.0 to 14.2)
T1:PMB2001(A56)-1:32(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 30.8)	0.0 (0.0 to 7.7)	2.0 (0.1 to 10.9)	0.0 (0.0 to 14.2)
T1:PMB2001(A56)-1:64(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 30.8)	0.0 (0.0 to 7.7)	0.0 (0.0 to 7.3)	0.0 (0.0 to 14.2)
T1:PMB2001(A56)-1:128,n=9,10,19,46,49,95,24,29,53	0.0 (0.0 to 30.8)	0.0 (0.0 to 7.7)	0.0 (0.0 to 7.3)	0.0 (0.0 to 14.2)
T1:PMB2948(B24)-1:4(n=10,11,21,46,51,97,31,30,61)	9.1 (0.2 to 41.3)	2.2 (0.1 to 11.5)	2.0 (0.0 to 10.4)	0.0 (0.0 to 11.2)
T1:PMB2948(B24)-1:8(n=10,11,21,46,51,97,31,30,61)	9.1 (0.2 to 41.3)	2.2 (0.1 to 11.5)	2.0 (0.0 to 10.4)	0.0 (0.0 to 11.2)
T1:PMB2948(B24)-1:16,n=10,11,21,46,51,97,31,30,61	9.1 (0.2 to 41.3)	2.2 (0.1 to 11.5)	2.0 (0.0 to 10.4)	0.0 (0.0 to 11.2)
T1:PMB2948(B24)-1:32,n=10,11,21,46,51,97,31,30,61	9.1 (0.2 to 41.3)	0.0 (0.0 to 7.7)	0.0 (0.0 to 7.0)	0.0 (0.0 to 11.2)
T1:PMB2948(B24)-1:64,n=10,11,21,46,51,97,31,30,61	0.0 (0.0 to 28.5)	0.0 (0.0 to 7.7)	0.0 (0.0 to 7.0)	0.0 (0.0 to 11.2)
T1:PMB2948(B24)-1:128n=10,11,21,46,51,97,31,30,61	0.0 (0.0 to 28.5)	0.0 (0.0 to 7.7)	0.0 (0.0 to 7.0)	0.0 (0.0 to 11.2)
T1:PMB2707(B44)-1:4(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 30.8)	2.2 (0.1 to 11.5)	0.0 (0.0 to 7.3)	0.0 (0.0 to 14.2)
T1:PB2707(B44)-1:8(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 30.8)	2.2 (0.1 to 11.5)	0.0 (0.0 to 7.3)	0.0 (0.0 to 14.2)
T1:PMB2707(B44)-1:16(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 30.8)	0.0 (0.0 to 7.7)	0.0 (0.0 to 7.3)	0.0 (0.0 to 14.2)
T1:PMB2707(B44)-1:32(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 30.8)	0.0 (0.0 to 7.7)	0.0 (0.0 to 7.3)	0.0 (0.0 to 14.2)

T1:PMB2707(B44)-1:64(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 30.8)	0.0 (0.0 to 7.7)	0.0 (0.0 to 7.3)	0.0 (0.0 to 14.2)
T1:PMB2707(B44)-1:128,n=9,10,19,46,49,95,24,30,54	0.0 (0.0 to 30.8)	0.0 (0.0 to 7.7)	0.0 (0.0 to 7.3)	0.0 (0.0 to 14.2)
T2:PMB80[A22]-1:4(n=10,9,19,45,50,95,30,29,59)	66.7 (29.9 to 92.5)	64.4 (48.8 to 78.1)	86.0 (73.3 to 94.2)	0.0 (0.0 to 11.6)
T2:PMB80[A22]-1:8(n=10,9,19,45,50,95,30,29,59)	66.7 (29.9 to 92.5)	64.4 (48.8 to 78.1)	86.0 (73.3 to 94.2)	0.0 (0.0 to 11.6)
T2:PMB80[A22]-1:32(n=10,9,19,45,50,95,30,29,59)	44.4 (13.7 to 78.8)	51.1 (35.8 to 66.3)	66.0 (51.2 to 78.8)	0.0 (0.0 to 11.6)
T2:PMB80[A22]-1:64(n=10,9,19,45,50,95,30,29,59)	22.2 (2.8 to 60.0)	28.9 (16.4 to 44.3)	40.0 (26.4 to 54.8)	0.0 (0.0 to 11.6)
T2:PMB80[A22]-1:128(n=10,9,19,45,50,95,30,29,59)	22.2 (2.8 to 60.0)	11.1 (3.7 to 24.1)	16.0 (7.2 to 29.1)	0.0 (0.0 to 11.6)
T2:PMB200[A56]-1:4(n=9,10,19,47,48,95,23,29,52)	100.0 (69.2 to 100.0)	100.0 (92.5 to 100.0)	100.0 (92.6 to 100.0)	4.3 (0.1 to 21.9)
T2:PMB2001[A56]-1:16(n=9,10,19,47,48,95,23,29,52)	90.0 (55.5 to 99.7)	100.0 (92.5 to 100.0)	100.0 (92.6 to 100.0)	0.0 (0.0 to 14.8)
T2:PMB2001[A56]-1:32(n=9,10,19,47,48,95,23,29,52)	90.0 (55.5 to 99.7)	95.7 (85.5 to 99.5)	95.8 (85.7 to 99.5)	0.0 (0.0 to 14.8)
T2:PMB2001[A56]-1:64(n=9,10,19,47,48,95,23,29,52)	70.0 (34.8 to 93.3)	87.2 (74.3 to 95.2)	85.4 (72.2 to 93.9)	0.0 (0.0 to 14.8)
T2:PMB2001[A56]-1:128,n=9,10,19,47,48,95,23,29,52	50.0 (18.7 to 81.3)	59.6 (44.3 to 73.6)	54.2 (39.2 to 68.8)	0.0 (0.0 to 14.8)
T2:PMB2948(B24)-1:4(n=10,9,19,42,44,86,30,29,59)	44.4 (13.7 to 78.8)	28.6 (15.7 to 44.6)	43.2 (28.3 to 59.0)	0.0 (0.0 to 11.6)
T2:PMB2948(B24)-1:16(n=10,9,19,42,44,86,30,29,59)	33.3 (7.5 to 70.1)	21.4 (10.3 to 36.8)	43.2 (28.3 to 59.0)	0.0 (0.0 to 11.6)
T2:PMB2948(B24)-1:32(n=10,9,19,42,44,86,30,29,59)	0.0 (0.0 to 33.6)	9.5 (2.7 to 22.6)	18.2 (8.2 to 32.7)	0.0 (0.0 to 11.6)
T2:PMB2948(B24)-1:64(n=10,9,19,42,44,86,30,29,59)	0.0 (0.0 to 33.6)	2.4 (0.1 to 12.6)	4.5 (0.6 to 15.5)	0.0 (0.0 to 11.6)
T2:PMB2948(B24)-1:128,n=10,9,19,42,44,86,30,29,59	0.0 (0.0 to 33.6)	2.4 (0.1 to 12.6)	0.0 (0.0 to 8.0)	0.0 (0.0 to 11.6)
T2:PMB2707(B44)-1:4(n=9,10,19,47,47,94,23,29,52)	70.0 (34.8 to 93.3)	72.3 (57.4 to 84.4)	63.8 (48.5 to 77.3)	0.0 (0.0 to 14.8)
T2:PMB2707(B44)-1:16(n=9,10,19,47,47,94,23,29,52)	60.0 (26.2 to 87.8)	72.3 (57.4 to 84.4)	61.7 (46.4 to 75.5)	0.0 (0.0 to 14.8)
T2:PMB2707(B44)-1:32(n=9,10,19,47,47,94,23,29,52)	60.0 (26.2 to 87.8)	61.7 (46.4 to 75.5)	51.1 (36.1 to 65.9)	0.0 (0.0 to 14.8)
T2:PMB2707(B44)-1:64(n=9,10,19,47,47,94,23,29,52)	30.0 (6.7 to 65.2)	27.7 (15.6 to 42.6)	21.3 (10.7 to 35.7)	0.0 (0.0 to 14.8)
T2:PMB270(B44)-1:128(n=9,10,19,47,47,94,23,29,52)	10.0 (0.3 to 44.5)	10.6 (3.5 to 23.1)	10.6 (3.5 to 23.1)	0.0 (0.0 to 14.8)
T3:PMB80(A22)-1:4(n=9,11,20,45,51,96,31,29,60)	90.9 (58.7 to 99.8)	91.1 (78.8 to 97.5)	88.2 (76.1 to 95.6)	6.5 (0.8 to 21.4)
T3:PMB80(A22)-1:8(n=9,11,20,45,51,96,31,29,60)	90.9 (58.7 to 99.8)	91.1 (78.8 to 97.5)	88.2 (76.1 to 95.6)	6.5 (0.8 to 21.4)
T3:PMB80(A22)-1:32(n=9,11,20,45,51,96,31,29,60)	81.8 (48.2 to 97.7)	82.2 (67.9 to 92.0)	86.3 (73.7 to 94.3)	3.2 (0.1 to 16.7)
T3:PMB80(A22)-1:64(n=9,11,20,45,51,96,31,29,60)	72.7 (39.0 to 94.0)	60.0 (44.3 to 74.3)	72.5 (58.3 to 84.1)	3.2 (0.1 to 16.7)
T3:PMB80(A22)-1:128(n=9,11,20,45,51,96,31,29,60)	54.5 (23.4 to 83.3)	37.8 (23.8 to 53.5)	49.0 (34.8 to 63.4)	0.0 (0.0 to 11.2)
T3:PMB2001(A56)-1:4(n=9,10,19,47,48,95,24,30,54)	100.0 (69.2 to 100.0)	100.0 (92.5 to 100.0)	100.0 (92.6 to 100.0)	8.3 (1.0 to 27.0)
T3:PMB2001(A56)-1:16(n=9,10,19,47,48,95,24,30,54)	100.0 (69.2 to 100.0)	97.9 (88.7 to 99.9)	100.0 (92.6 to 100.0)	0.0 (0.0 to 14.2)
T3:PMB2001(A56)-1:32(n=9,10,19,47,48,95,24,30,54)	90.0 (55.5 to 99.7)	97.9 (88.7 to 99.9)	93.8 (82.8 to 98.7)	0.0 (0.0 to 14.2)
T3:PMB2001(A56)-1:64(n=9,10,19,47,48,95,24,30,54)	80.0 (44.4 to 97.5)	93.6 (82.5 to 98.7)	85.4 (72.2 to 93.9)	0.0 (0.0 to 14.2)

T3:PMB2001(A56)-1:128,n=9,10,19,47,48,95,24,30,54	80.0 (44.4 to 97.5)	89.4 (76.9 to 96.5)	77.1 (62.7 to 88.0)	0.0 (0.0 to 14.2)
T3:PMB2948(B24)-1:4(n=9,11,20,45,50,95,31,29,60)	81.8 (48.2 to 97.7)	71.1 (55.7 to 83.6)	72.0 (57.5 to 83.8)	3.2 (0.1 to 16.7)
T3:PMB2948(B24)-1:16(n=9,11,20,45,50,95,31,29,60)	63.6 (30.8 to 89.1)	66.7 (51.0 to 80.0)	68.0 (53.3 to 80.5)	3.2 (0.1 to 16.7)
T3:PMB2948(B24)-1:32(n=9,11,20,45,50,95,31,29,60)	36.4 (10.9 to 69.2)	37.8 (23.8 to 53.5)	34.0 (21.2 to 48.8)	3.2 (0.1 to 16.7)
T3:PMB2948(B24)-1:64(n=9,11,20,45,50,95,31,29,60)	18.2 (2.3 to 51.8)	17.8 (8.0 to 32.1)	10.0 (3.3 to 21.8)	0.0 (0.0 to 11.2)
T3:PMB2948(B24)-1:128,n=9,11,20,45,50,95,31,29,60	9.1 (0.2 to 41.3)	2.2 (0.1 to 11.8)	2.0 (0.1 to 10.6)	0.0 (0.0 to 11.2)
T3:PMB2707(B44)-1:4(n=9,10,19,47,47,94,24,30,54)	90.0 (55.5 to 99.7)	87.2 (74.3 to 95.2)	87.2 (74.3 to 95.2)	0.0 (0.0 to 14.2)
T3:PMB2707(B44)-1:16(n=9,10,19,47,47,94,24,30,54)	90.0 (55.5 to 99.7)	87.2 (74.3 to 95.2)	85.1 (71.7 to 93.8)	0.0 (0.0 to 14.2)
T3:PMB2707(B44)-1:32(n=9,10,19,47,47,94,24,30,54)	70.0 (34.8 to 93.3)	74.5 (59.7 to 86.1)	78.7 (64.3 to 89.3)	0.0 (0.0 to 14.2)
T3:PMB2707(B44)-1:64(n=9,10,19,47,47,94,24,30,54	30.0 (6.7 to 65.2)	57.4 (42.2 to 71.7)	59.6 (44.3 to 73.6)	0.0 (0.0 to 14.2)
T3:PMB2707(B44)-1:128,n=9,10,19,47,47,94,24,30,54	20.0 (2.5 to 55.6)	29.8 (17.3 to 44.9)	34.0 (20.9 to 49.3)	0.0 (0.0 to 14.2)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: percentage of subjects				
number (confidence interval 95%)				
T1:PMB80[A22]-1:4(n=9,11,20,46,51,97,31,30,61)	3.3 (0.1 to 17.2)			
T1:PMB80[A22]-1:8(n=9,11,20,46,51,97,31,30,61)	3.3 (0.1 to 17.2)			
T1:PMB80[A22]-1:16(n=9,11,20,46,51,97,31,30,61)	3.3 (0.1 to 17.2)			
T1:PMB80[A22]-1:32(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 11.6)			
T1:PMB80[A22]-1:64(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 11.6)			
T1:PMB80[A22]-1:128(n=9,11,20,46,51,97,31,30,61)	0.0 (0.0 to 11.6)			
T1:PMB2001(A56)-1:4(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 11.9)			
T1:PMB2001(A56)-1:8(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 11.9)			
T1:PMB2001(A56)-1:16(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 11.9)			
T1:PMB2001(A56)-1:32(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 11.9)			
T1:PMB2001(A56)-1:64(n=9,10,19,46,49,95,24,29,53)	0.0 (0.0 to 11.9)			
T1:PMB2001(A56)-1:128,n=9,10,19,46,49,95,24,29,53	0.0 (0.0 to 11.9)			
T1:PMB2948(B24)-1:4(n=10,11,21,46,51,97,31,30,61)	3.3 (0.1 to 17.2)			

T1:PMB2948(B24)-1:8(n=10,11,21,46,51,97,31,30,61)	3.3 (0.1 to 17.2)			
T1:PMB2948(B24)-1:16,n=10,11,21,46,51,97,31,30,61	3.3 (0.1 to 17.2)			
T1:PMB2948(B24)-1:32,n=10,11,21,46,51,97,31,30,61	3.3 (0.1 to 17.2)			
T1:PMB2948(B24)-1:64,n=10,11,21,46,51,97,31,30,61	3.3 (0.1 to 17.2)			
T1:PMB2948(B24)-1:128n=10,11,21,46,51,97,31,30,61	0.0 (0.0 to 11.6)			
T1:PMB2707(B44)-1:4(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 11.6)			
T1:PB2707(B44)-1:8(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 11.6)			
T1:PMB2707(B44)-1:16(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 11.6)			
T1:PMB2707(B44)-1:32(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 11.6)			
T1:PMB2707(B44)-1:64(n=9,10,19,46,49,95,24,30,54)	0.0 (0.0 to 11.6)			
T1:PMB2707(B44)-1:128,n=9,10,19,46,49,95,24,30,54	0.0 (0.0 to 11.6)			
T2:PMB80[A22]-1:4(n=10,9,19,45,50,95,30,29,59)	3.4 (0.1 to 17.8)			
T2:PMB80[A22]-1:8(n=10,9,19,45,50,95,30,29,59)	3.4 (0.1 to 17.8)			
T2:PMB80[A22]-1:32(n=10,9,19,45,50,95,30,29,59)	3.4 (0.1 to 17.8)			
T2:PMB80[A22]-1:64(n=10,9,19,45,50,95,30,29,59)	3.4 (0.1 to 17.8)			
T2:PMB80[A22]-1:128(n=10,9,19,45,50,95,30,29,59)	0.0 (0.0 to 11.9)			
T2:PMB200[A56]-1:4(n=9,10,19,47,48,95,23,29,52)	0.0 (0.0 to 11.9)			
T2:PMB2001[A56]-1:16(n=9,10,19,47,48,95,23,29,52)	0.0 (0.0 to 11.9)			
T2:PMB2001[A56]-1:32(n=9,10,19,47,48,95,23,29,52)	0.0 (0.0 to 11.9)			
T2:PMB2001[A56]-1:64(n=9,10,19,47,48,95,23,29,52)	0.0 (0.0 to 11.9)			
T2:PMB2001[A56]-1:128,n=9,10,19,47,48,95,23,29,52	0.0 (0.0 to 11.9)			
T2:PMB2948(B24)-1:4(n=10,9,19,42,44,86,30,29,59)	3.4 (0.1 to 17.8)			
T2:PMB2948(B24)-1:16(n=10,9,19,42,44,86,30,29,59)	3.4 (0.1 to 17.8)			
T2:PMB2948(B24)-1:32(n=10,9,19,42,44,86,30,29,59)	3.4 (0.1 to 17.8)			
T2:PMB2948(B24)-1:64(n=10,9,19,42,44,86,30,29,59)	0.0 (0.0 to 11.9)			
T2:PMB2948(B24)-1:128,n=10,9,19,42,44,86,30,29,59	0.0 (0.0 to 11.9)			
T2:PMB2707(B44)-1:4(n=9,10,19,47,47,94,23,29,52)	0.0 (0.0 to 11.9)			
T2:PMB2707(B44)-1:16(n=9,10,19,47,47,94,23,29,52)	0.0 (0.0 to 11.9)			
T2:PMB2707(B44)-1:32(n=9,10,19,47,47,94,23,29,52)	0.0 (0.0 to 11.9)			
T2:PMB2707(B44)-1:64(n=9,10,19,47,47,94,23,29,52)	0.0 (0.0 to 11.9)			
T2:PMB270(B44)-1:128(n=9,10,19,47,47,94,23,29,52)	0.0 (0.0 to 11.9)			

T3:PMB80(A22)-1:4(n=9,11,20,45,51,96,31,29,60)	6.9 (0.8 to 22.8)			
T3:PMB80(A22)-1:8(n=9,11,20,45,51,96,31,29,60)	6.9 (0.8 to 22.8)			
T3:PMB80(A22)-1:32(n=9,11,20,45,51,96,31,29,60)	3.4 (0.1 to 17.8)			
T3:PMB80(A22)-1:64(n=9,11,20,45,51,96,31,29,60)	0.0 (0.0 to 11.9)			
T3:PMB80(A22)-1:128(n=9,11,20,45,51,96,31,29,60)	0.0 (0.0 to 11.9)			
T3:PMB2001(A56)-1:4(n=9,10,19,47,48,95,24,30,54)	10.0 (2.1 to 26.5)			
T3:PMB2001(A56)-1:16(n=9,10,19,47,48,95,24,30,54)	3.3 (0.1 to 7.2)			
T3:PMB2001(A56)-1:32(n=9,10,19,47,48,95,24,30,54)	3.3 (0.1 to 17.2)			
T3:PMB2001(A56)-1:64(n=9,10,19,47,48,95,24,30,54)	0.0 (0.0 to 11.6)			
T3:PMB2001(A56)-1:128,n=9,10,19,47,48,95,24,30,54	0.0 (0.0 to 11.6)			
T3:PMB2948(B24)-1:4(n=9,11,20,45,50,95,31,29,60)	6.9 (0.8 to 22.8)			
T3:PMB2948(B24)-1:16(n=9,11,20,45,50,95,31,29,60)	6.9 (0.8 to 22.8)			
T3:PMB2948(B24)-1:32(n=9,11,20,45,50,95,31,29,60)	0.0 (0.0 to 11.9)			
T3:PMB2948(B24)-1:64(n=9,11,20,45,50,95,31,29,60)	0.0 (0.0 to 11.9)			
T3:PMB2948(B24)-1:128,n=9,11,20,45,50,95,31,29,60	0.0 (0.0 to 11.9)			
T3:PMB2707(B44)-1:4(n=9,10,19,47,47,94,24,30,54)	0.0 (0.0 to 11.6)			
T3:PMB2707(B44)-1:16(n=9,10,19,47,47,94,24,30,54)	0.0 (0.0 to 11.6)			
T3:PMB2707(B44)-1:32(n=9,10,19,47,47,94,24,30,54)	0.0 (0.0 to 11.6)			
T3:PMB2707(B44)-1:64(n=9,10,19,47,47,94,24,30,54	0.0 (0.0 to 11.6)			
T3:PMB2707(B44)-1:128,n=9,10,19,47,47,94,24,30,54	0.0 (0.0 to 11.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Bactericidal Assay Using Human Complement (hSBA) Geometric Mean Titers (GMTs) for Each of the 4 Primary Test Strains

End point title	Serum Bactericidal Assay Using Human Complement (hSBA) Geometric Mean Titers (GMTs) for Each of the 4 Primary Test Strains

End point description:

Percentage of subjects achieving hSBA titer >= LLOQ were computed along with corresponding 2-sided 95% CIs. LLOQ was 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44). Evaluable immunogenicity population: all eligible subjects randomized to study received,scheduled investigational products, had pre and post vaccination blood drawn with valid and determinate assay results and had no important protocol deviation. Here, N signifies number of subjects evaluable for this endpoint and n signifies number of subjects analyzed at specific time points only. Here, 99999 represents that CI was not estimable due to the lack of variability of geometric means.

End point type	Secondary

End point timeframe:

Before Vaccination 1 (T1), 1 month after Vaccination 2 (T2), 1 month after Vaccination 3 (T3)

End point values	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 1: 60-µg bivalent rLP2086 (>=12 months to <18 months)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	21	97	61	10
Units: titers				
geometric mean (confidence interval 95%)				
T1:PMB80(A22(n=9,11,20,46,51,97,31, 30,61)	8.0 (-99999 to 99999)	8.4 (7.9 to 9.0)	8.1 (7.9 to 8.3)	8.0 (-99999 to 99999)
T1:PMB2001(A56)(n=9,10,19,46,49,95, 24,29,53)	4.0 (-99999 to 99999)	4.1 (3.9 to 4.3)	4.0 (-99999 to 99999)	4.0 (-99999 to 99999)
T1:PMB2948(B24)(n=10, 11,21,46,51,97,31,30,61)	4.4 (3.6 to 5.4)	4.1 (4.0 to 4.3)	4.2 (3.8 to 4.6)	4.0 (-99999 to 99999)
T1:PMB2707(B44)(n=9,10,19,46,49,95, 24, 30,54)	4.0 (-99999 to 99999)	4.0 (4.0 to 4.1)	4.0 (-99999 to 99999)	4.0 (-99999 to 99999)
T2:PMB80(A22)(n=10,9,19,45,50,95,30 ,29,59)	32.0 (19.7 to 52.0)	30.4 (24.3 to 38.1)	8.3 (7.7 to 8.9)	42.2 (22.6 to 79.1)
T2:PMB2001(A56)(n =9,10,19,47,48,95,23,29,52)	82.6 (51.4 to 132.9)	110.6 (92.0 to 133.0)	4.0 (-99999 to 99999)	101.6 (64.0 to 161.2)
T2:PMB2948(B24)(n =10,9,19,42,44,86,30,29,59)	8.6 (6.1 to 12.2)	7.2 (5.9 to 8.7)	4.1 (3.9 to 4.4)	10.6 (6.2 to 18.0)
T2:PMB2707(B44)(n=9,10,19,47,47,94, 23,29,52)	22.2 (11.2 to 43.9)	19.4 (15.1 to 24.9)	40 (-99999 to 99999)	23.5 (9.3 to 59.4)
T3:PMB80(A22)(n=9,11,20,45,51,96,31 ,29,60)	81.6 (46.6 to 142.8)	67.3 (53.7 to 84.3)	8.6 (7.9 to 9.3)	80.6 (30.9 to 210.7)
T3:PMB2001(A56)(n=9, 10,19,47,48,95,24,30,54)	142.8 (85.5 to 238.6)	171.4 (141.6 to 207.4)	4.2 (3.8 to 4.5)	109.7 (70.4 to 171.1)
T3:PMB2948(B24)(n =9,11,20,45,50,95,31, 29,60)	18.4 (11.8 to 28.6)	15.1 (12.3 to 18.6)	4.3 (3.9 to 4.8)	20.2 (11.1 to 36.6)
T3:PMB2707(B44)(n =9,10,19,47,94,24,30,54)	32.0 (18.3 to 55.8)	45.6 (35.2 to 59.0)	4.0 (-99999 to 99999)	29.6 (11.6 to 75.8)

End point values	Group 1: 60-µg bivalent rLP2086 (>=18 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <18 months)	Group 2: 120-µg bivalent rLP2086 (>=18 months to <24 months)	Group 3: HAV/Saline (>=12 months to <18 months)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	47	51	31
Units: titers				
geometric mean (confidence interval 95%)				
T1:PMB80(A22(n=9,11,20,46,51,97,31, 30,61)	8.0 (-99999 to 99999)	8.5 (7.5 to 9.6)	8.3 (7.8 to 8.9)	8.0 (-99999 to 99999)
T1:PMB2001(A56)(n=9,10,19,46,49,95, 24,29,53)	4.0 (-99999 to 99999)	4.0 (-99999 to 99999)	4.2 (3.8 to 4.5)	4.0 (-99999 to 99999)

T1:PMB2948(B24)(n=10, 11,21,46,51,97,31,30,61)	4.8 (3.2 to 7.4)	4.1 (3.9 to 4.4)	4.1 (3.9 to 4.3)	4.0 (-99999 to 99999)
T1:PMB2707(B44)(n=9,10,19,46,49,95, 24, 30,54)	4.0 (-99999 to 99999)	4.1 (3.9 to 4.2)	4.0 (-99999 to 99999)	4.0 (-99999 to 99999)
T2:PMB80(A22)(n=10,9,19,45,50,95,30 ,29,59)	23.5 (10.1 to 54.9)	24.6 (17.8 to 34.2)	36.8 (26.9 to 50.3)	8.0 (-99999 to 99999)
T2:PMB2001(A56)(n =9,10,19,47,48,95,23,29,52)	68.6 (28.2 to 166.8)	117.2 (89.7 to 153.0)	104.6 (80.4 to 136.0)	4.0 (-99999 to 99999)
T2:PMB2948(B24)(n =10,9,19,42,44,86,30,29,59)	6.9 (4.1 to 11.5)	6.0 (4.7 to 7.8)	8.5 (6.4 to 11.3)	4.0 (-99999 to 99999)
T2:PMB2707(B44)(n=9,10,19,47,47,94, 23,29,52)	21.1 (6.5 to 68.3)	22.1 (15.5 to 31.6)	17.0 (11.8 to 24.4)	4.0 (-99999 to 99999)
T3:PMB80(A22)(n=9,11,20,45,51,96,31 ,29,60)	82.3 (36.5 to 185.8)	63.0 (44.5 to 89.3)	71.4 (52.7 to 96.6)	8.6 (7.5 to 9.8)
T3:PMB2001(A56)(n=9, 10,19,47,48,95,24,30,54)	181.0 (68.6 to 477.9)	190.6 (146.9 to 247.4)	154.4 (116.3 to 205.1)	4.0 (-99999 to 99999)
T3:PMB2948(B24)(n =9,11,20,45,50,95,31, 29,60)	17.0 (8.2 to 35.5)	15.8 (11.4 to 21.8)	14.5 (11.1 to 19.1)	4.3 (3.7 to 4.9)
T3:PMB2707(B44)(n =9,10,19,47,94,24,30,54)	34.3 (15.0 to 78.2)	46.3 (31.6 to 67.8)	44.9 (31.3 to 64.5)	4.0 (-99999 to 99999)

End point values	Group 3: HAV/Saline (>=18 months to <24 months)			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: titers				
geometric mean (confidence interval 95%)				
T1:PMB80(A22(n=9,11,20,46,51,97,31, 30,61)	8.2 (7.8 to 8.8)			
T1:PMB2001(A56)(n=9,10,19,46,49,95, 24,29,53)	4.0 (-99999 to 99999)			
T1:PMB2948(B24)(n=10, 11,21,46,51,97,31,30,61)	4.4 (3.6 to 5.3)			
T1:PMB2707(B44)(n=9,10,19,46,49,95, 24, 30,54)	4.0 (-99999 to 99999)			
T2:PMB80(A22)(n=10,9,19,45,50,95,30 ,29,59)	8.6 (7.4 to 10.0)			
T2:PMB2001(A56)(n =9,10,19,47,48,95,23,29,52)	4.0 (-99999 to 99999)			
T2:PMB2948(B24)(n =10,9,19,42,44,86,30,29,59)	4.3 (3.7 to 5.0)			
T2:PMB2707(B44)(n=9,10,19,47,47,94, 23,29,52)	4.0 (-99999 to 99999)			
T3:PMB80(A22)(n=9,11,20,45,51,96,31 ,29,60)	8.6 (7.7 to 9.6)			
T3:PMB2001(A56)(n=9, 10,19,47,48,95,24,30,54)	4.3 (3.7 to 4.9)			
T3:PMB2948(B24)(n =9,11,20,45,50,95,31, 29,60)	4.4 (3.8 to 5.0)			
T3:PMB2707(B44)(n =9,10,19,47,94,24,30,54)	4.0 (-99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs: Recorded from Vaccination 1 through 6 months after Vaccination 3. Subjects recorded local reactions and systemic events in e-diary within 7 days after Vaccination 1, 2 and 3. NSAEs: Recorded from Vaccination 1 through 1 month after Vaccination 3.

Adverse event reporting additional description:

SAEs and AEs were grouped by system organ class and preferred term. AEs included AEs collected in the e-diary (local and systemic reactions; systematic assessment) and AEs collected on the case report form at each visit (nonsystematic assessment).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)

Reporting group description:

Subjects from >=12 months to <24 months of age, received intramuscular injection of 60 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.

Reporting group title	Group 3: HAV/Saline (>=12 months to <24 months)

Reporting group description:

Subjects from >=12 months to <24 months of age, received intramuscular injection of saline on 2-month and HAV vaccine on a 0-, 6- month schedule.

Reporting group title	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)

Reporting group description:

Subjects from >=12 months to <24 months of age, received intramuscular injection of 120 µg of bivalent rLP2086 vaccine on a 0-, 2-, 6- month schedule.

Serious adverse events	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 44 (9.09%)	8 / 132 (6.06%)	19 / 220 (8.64%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Accidental exposure to product			
subjects affected / exposed	0 / 44 (0.00%)	1 / 132 (0.76%)	0 / 220 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			

subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar ataxia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Crying			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eyelid ptosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 44 (0.00%)	1 / 132 (0.76%)	0 / 220 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 132 (0.76%)	0 / 220 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polydipsia psychogenic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	2 / 220 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Croup infectious			
subjects affected / exposed	0 / 44 (0.00%)	1 / 132 (0.76%)	0 / 220 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovirus infection			
subjects affected / exposed	0 / 44 (0.00%)	1 / 132 (0.76%)	0 / 220 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 132 (0.76%)	3 / 220 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	2 / 220 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	3 / 220 (1.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			

subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	2 / 220 (0.91%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral tonsillitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	2 / 220 (0.91%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 44 (0.00%)	1 / 132 (0.76%)	0 / 220 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Group 1: 60-µg bivalent rLP2086 (>=12 months to <24 months)	Group 3: HAV/Saline (>=12 months to <24 months)	Group 2: 120-µg bivalent rLP2086 (>=12 months to <24 months)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 44 (97.73%)	113 / 132 (85.61%)	209 / 220 (95.00%)
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	3 / 220 (1.36%)
occurrences (all)	0	0	3
Injection site erythema			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Injection site erythema (redness)			
alternative assessment type: Systematic			
subjects affected / exposed	30 / 44 (68.18%)	28 / 132 (21.21%)	137 / 220 (62.27%)
occurrences (all)	59	40	249
Injection site pain (tenderness at			

injection site)			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 44 (79.55%)	41 / 132 (31.06%)	160 / 220 (72.73%)
occurrences (all)	72	62	361
Injection site pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	4 / 220 (1.82%)
occurrences (all)	1	0	5
Injection site swelling (swelling)			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 44 (38.64%)	20 / 132 (15.15%)	103 / 220 (46.82%)
occurrences (all)	33	26	154
Pyrexia			
subjects affected / exposed	1 / 44 (2.27%)	6 / 132 (4.55%)	18 / 220 (8.18%)
occurrences (all)	1	6	18
Vaccination site pain			
subjects affected / exposed	1 / 44 (2.27%)	1 / 132 (0.76%)	2 / 220 (0.91%)
occurrences (all)	1	1	2
Vessel puncture site bruise			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Pyrexia (fever)			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 44 (36.36%)	20 / 132 (15.15%)	82 / 220 (37.27%)
occurrences (all)	23	22	118
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 44 (2.27%)	3 / 132 (2.27%)	8 / 220 (3.64%)
occurrences (all)	1	3	9
Rhinorrhoea			
subjects affected / exposed	2 / 44 (4.55%)	2 / 132 (1.52%)	11 / 220 (5.00%)
occurrences (all)	2	3	14
Rhinitis allergic			

subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	2 / 220 (0.91%)
occurrences (all)	1	0	3
Psychiatric disorders			
Irritability			
subjects affected / exposed	5 / 44 (11.36%)	5 / 132 (3.79%)	21 / 220 (9.55%)
occurrences (all)	6	7	31
Irritability1			
alternative assessment type: Systematic			
subjects affected / exposed	31 / 44 (70.45%)	69 / 132 (52.27%)	176 / 220 (80.00%)
occurrences (all)	61	116	369
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 44 (0.00%)	1 / 132 (0.76%)	3 / 220 (1.36%)
occurrences (all)	0	1	4
Arthropod sting			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Concussion			
subjects affected / exposed	0 / 44 (0.00%)	3 / 132 (2.27%)	0 / 220 (0.00%)
occurrences (all)	0	3	0
Contusion			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	5 / 220 (2.27%)
occurrences (all)	0	2	6
Craniocerebral injury			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	0 / 220 (0.00%)
occurrences (all)	0	2	0
Excoriation			
subjects affected / exposed	1 / 44 (2.27%)	1 / 132 (0.76%)	0 / 220 (0.00%)
occurrences (all)	1	1	0
Face injury			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	0 / 220 (0.00%)
occurrences (all)	0	2	0
Fall			
subjects affected / exposed	2 / 44 (4.55%)	7 / 132 (5.30%)	5 / 220 (2.27%)
occurrences (all)	2	9	6
Hand fracture			

subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Laceration			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	4 / 220 (1.82%)
occurrences (all)	1	0	4
Lip injury			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	3 / 220 (1.36%)
occurrences (all)	0	0	3
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	2	0	0
Somnolence (drowsiness)			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 44 (52.27%)	40 / 132 (30.30%)	127 / 220 (57.73%)
occurrences (all)	32	56	234
Somnolence			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	3 / 220 (1.36%)
occurrences (all)	0	3	3
Ear and labyrinth disorders			
Eustachian tube disorder			
subjects affected / exposed	1 / 44 (2.27%)	1 / 132 (0.76%)	1 / 220 (0.45%)
occurrences (all)	1	1	1
Middle ear effusion			
subjects affected / exposed	0 / 44 (0.00%)	3 / 132 (2.27%)	8 / 220 (3.64%)
occurrences (all)	0	4	9
Eye disorders			
Anisometropia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Astigmatism			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis allergic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0

Hypermetropia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Aphthous ulcer			
subjects affected / exposed	3 / 44 (6.82%)	0 / 132 (0.00%)	1 / 220 (0.45%)
occurrences (all)	3	0	1
Diarrhoea			
subjects affected / exposed	1 / 44 (2.27%)	5 / 132 (3.79%)	11 / 220 (5.00%)
occurrences (all)	2	6	15
Enteritis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Teething			
subjects affected / exposed	0 / 44 (0.00%)	4 / 132 (3.03%)	8 / 220 (3.64%)
occurrences (all)	0	5	10
Vomiting			
subjects affected / exposed	1 / 44 (2.27%)	5 / 132 (3.79%)	8 / 220 (3.64%)
occurrences (all)	1	5	8
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	1 / 44 (2.27%)	2 / 132 (1.52%)	4 / 220 (1.82%)
occurrences (all)	1	2	4
Dermatitis contact			
subjects affected / exposed	0 / 44 (0.00%)	1 / 132 (0.76%)	4 / 220 (1.82%)
occurrences (all)	0	1	4
Dermatitis diaper			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	3 / 220 (1.36%)
occurrences (all)	0	0	3
Dermatitis			
subjects affected / exposed	0 / 44 (0.00%)	3 / 132 (2.27%)	3 / 220 (1.36%)
occurrences (all)	0	3	3
Eczema			

subjects affected / exposed	0 / 44 (0.00%)	4 / 132 (3.03%)	4 / 220 (1.82%)
occurrences (all)	0	4	4
Miliaria			
subjects affected / exposed	1 / 44 (2.27%)	1 / 132 (0.76%)	1 / 220 (0.45%)
occurrences (all)	2	1	1
Rash generalised			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 44 (0.00%)	1 / 132 (0.76%)	3 / 220 (1.36%)
occurrences (all)	0	1	3
Urticaria			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	4 / 220 (1.82%)
occurrences (all)	0	2	5
Musculoskeletal and connective tissue disorders			
Synovitis			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	0 / 220 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	3 / 220 (1.36%)
occurrences (all)	0	2	4
Bronchitis			
subjects affected / exposed	5 / 44 (11.36%)	11 / 132 (8.33%)	22 / 220 (10.00%)
occurrences (all)	9	12	27
Cellulitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	2 / 220 (0.91%)
occurrences (all)	1	0	2
Conjunctivitis			
subjects affected / exposed	1 / 44 (2.27%)	13 / 132 (9.85%)	22 / 220 (10.00%)
occurrences (all)	1	15	23
Croup infectious			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	9 / 220 (4.09%)
occurrences (all)	0	2	9
Enterobiasis			

subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	2 / 220 (0.91%)
occurrences (all)	0	2	2
Gastroenteritis viral			
subjects affected / exposed	1 / 44 (2.27%)	3 / 132 (2.27%)	10 / 220 (4.55%)
occurrences (all)	1	4	12
Exanthema subitum			
subjects affected / exposed	0 / 44 (0.00%)	0 / 132 (0.00%)	3 / 220 (1.36%)
occurrences (all)	0	0	3
Gastroenteritis			
subjects affected / exposed	4 / 44 (9.09%)	11 / 132 (8.33%)	29 / 220 (13.18%)
occurrences (all)	5	11	35
Hand-foot-and-mouth disease			
subjects affected / exposed	2 / 44 (4.55%)	6 / 132 (4.55%)	10 / 220 (4.55%)
occurrences (all)	2	6	11
Impetigo			
subjects affected / exposed	1 / 44 (2.27%)	3 / 132 (2.27%)	3 / 220 (1.36%)
occurrences (all)	1	3	3
Laryngitis			
subjects affected / exposed	2 / 44 (4.55%)	5 / 132 (3.79%)	3 / 220 (1.36%)
occurrences (all)	3	5	3
Infected bite			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	2 / 220 (0.91%)
occurrences (all)	2	0	2
Lower respiratory tract infection			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	4 / 220 (1.82%)
occurrences (all)	0	2	4
Molluscum contagiosum			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	7 / 44 (15.91%)	7 / 132 (5.30%)	3 / 220 (1.36%)
occurrences (all)	8	11	4
Otitis externa			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	0 / 220 (0.00%)
occurrences (all)	0	2	0
Otitis media acute			

subjects affected / exposed	1 / 44 (2.27%)	2 / 132 (1.52%)	2 / 220 (0.91%)
occurrences (all)	1	2	2
Otitis media			
subjects affected / exposed	3 / 44 (6.82%)	20 / 132 (15.15%)	27 / 220 (12.27%)
occurrences (all)	3	32	38
Pharyngitis streptococcal			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	1 / 220 (0.45%)
occurrences (all)	0	2	1
Pharyngitis			
subjects affected / exposed	6 / 44 (13.64%)	15 / 132 (11.36%)	18 / 220 (8.18%)
occurrences (all)	7	18	19
Pharyngotonsillitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 44 (0.00%)	2 / 132 (1.52%)	7 / 220 (3.18%)
occurrences (all)	0	2	7
Respiratory tract infection viral			
subjects affected / exposed	2 / 44 (4.55%)	1 / 132 (0.76%)	3 / 220 (1.36%)
occurrences (all)	4	1	5
Respiratory tract infection			
subjects affected / exposed	0 / 44 (0.00%)	1 / 132 (0.76%)	4 / 220 (1.82%)
occurrences (all)	0	1	5
Rhinitis			
subjects affected / exposed	3 / 44 (6.82%)	3 / 132 (2.27%)	8 / 220 (3.64%)
occurrences (all)	3	4	11
Skin candida			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	0 / 220 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	4 / 44 (9.09%)	9 / 132 (6.82%)	6 / 220 (2.73%)
occurrences (all)	5	9	7
Tracheitis			
subjects affected / exposed	1 / 44 (2.27%)	5 / 132 (3.79%)	1 / 220 (0.45%)
occurrences (all)	1	6	1
Upper respiratory tract infection			

subjects affected / exposed	6 / 44 (13.64%)	34 / 132 (25.76%)	58 / 220 (26.36%)
occurrences (all)	9	61	103
Urinary tract infection			
subjects affected / exposed	0 / 44 (0.00%)	3 / 132 (2.27%)	7 / 220 (3.18%)
occurrences (all)	0	3	7
Varicella			
subjects affected / exposed	2 / 44 (4.55%)	3 / 132 (2.27%)	5 / 220 (2.27%)
occurrences (all)	2	3	5
Viral infection			
subjects affected / exposed	1 / 44 (2.27%)	2 / 132 (1.52%)	3 / 220 (1.36%)
occurrences (all)	1	2	3
Viral pharyngitis			
subjects affected / exposed	2 / 44 (4.55%)	1 / 132 (0.76%)	0 / 220 (0.00%)
occurrences (all)	2	1	0
Viral tonsillitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 132 (0.00%)	2 / 220 (0.91%)
occurrences (all)	1	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	5 / 44 (11.36%)	23 / 132 (17.42%)	45 / 220 (20.45%)
occurrences (all)	6	32	91
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 44 (2.27%)	2 / 132 (1.52%)	1 / 220 (0.45%)
occurrences (all)	1	4	1
Decreased appetite (loss of appetite)			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 44 (50.00%)	50 / 132 (37.88%)	142 / 220 (64.55%)
occurrences (all)	35	76	250

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 February 2015	Updation of description of control vaccine (pediatric HAV vaccine) and removal of references to a specific brand of control vaccine (Havrix Junior), clinical experience section for bivalent rLP2086, background section to include current licensure status of Bexsero and Trumenba, clarification of administration site instructions, correction of typographical errors related to data monitoring comittee (blinded to unblinded).
19 April 2016	Updation of unblinding strategy based on the actual enrollment rate, required freezer temperature for storing serum samples, adverse event reporting section, clarification of the performance of primary analysis and timing of stages of the study, incorporation of updates from administrative change letters of the date 02 September 2015 and 12 November 2015, deletion of appendix detailing the enrollment plan.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The data for the immunogenicity outcome measures at 6, 12, and 24 months after Vaccination 3 and 1 month after the Booster dose are not available due to lab delays. The results will be posted as soon as the data is available.

Notes: