Clinical trial results:
A Phase 3, Randomized, Active-Controlled, Observer-Blinded Trial to Assess the Lot Consistency, Safety, Tolerability, and Immunogenicity of a Meningococcal Serogroup B Bivalent rLP2086 Vaccine in Healthy Subjects Aged 10 to <19 Years

Summary

EudraCT number	2010-023873-20
Trial protocol	DE HU FI CZ GB ES PL IT Outside EU/EEA
Global end of trial date	14 April 2015

Results information

Result version number	v1 (current)
This version publication date	19 November 2016
First version publication date	19 November 2016

Trial information

Trial identification

Sponsor protocol code	B1971009

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01830855
WHO universal trial number (UTN)	-
Other trial identifiers	Alias: 6108A1-3001

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, 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	Final
Date of interim/final analysis	07 October 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety profile of bivalent recombinant lipoprotein 2086 (rLP2086) vaccine compared to a control (hepatitis A virus [HAV]/saline), as measured by local reactions, systemic events, adverse events (AEs), serious AEs, newly diagnosed chronic medical conditions, medically attended AEs, and immediate AEs. To assess the immune response as measured by serum bactericidal assay using human complement (hSBA) performed with 4 primary Neisseria meningitidis serogroup B (MnB) test 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 vaccine. To demonstrate that the immune responses induced by 3 lots of bivalent rLP2086 vaccine are equivalent as measured by hSBA performed with 2 primary MnB test strains, 1 expressing an LP2086 subfamily A protein and 1 expressing an LP2086 subfamily B protein, 1 month after the third vaccination with bivalent rLP2086 vaccine.

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 Conference on 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	18 April 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
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	Canada: 114
Country: Number of subjects enrolled	Czech Republic: 116
Country: Number of subjects enrolled	Finland: 589
Country: Number of subjects enrolled	Germany: 184
Country: Number of subjects enrolled	Italy: 184
Country: Number of subjects enrolled	Poland: 439
Country: Number of subjects enrolled	United States: 1805
Country: Number of subjects enrolled	United Kingdom: 159
Worldwide total number of subjects	3590
EEA total number of subjects	1671

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	849
Adolescents (12-17 years)	2346
Adults (18-64 years)	395
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 3596 subjects were randomized in this study, out of which 3590 subjects received vaccination.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 rLP2086 Lot 1

Arm description:

Lot 1 on a 0-, 2-, 6- month schedule.

Arm type	Experimental
Investigational medicinal product name	rLP2086 Lot 1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 1 dose of 0.5 milliliter (mL) of bivalent rLP2086 Lot 1 0-, 2-, and 6-month schedule.

Arm title	Group 2 rLP2086 Lot 2

Arm description:

Lot 2 on a 0-, 2-, 6- month schedule.

Arm type	Experimental
Investigational medicinal product name	rLP2086 Lot 2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 1 dose of 0.5 mL of bivalent rLP2086 Lot 2 0-, 2-, and 6-month schedule.

Arm title	Group 3 rLP2086 Lot 3

Arm description:

Lot 3 on a 0-, 2-, 6- month schedule.

Arm type	Experimental
Investigational medicinal product name	rLP2086 Lot 3
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 1 dose of 0.5 mL of bivalent rLP2086 Lot 3 on 0-, 2-, and 6-month schedule.

Arm title	Group 4 HAV/Saline
Arm description:	
Hepatitis A virus vaccine (HAV) on a 0- and 6-month schedule and saline at Month 2.	
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 received 1 dose 0.5 mL of HAV on 0- and 6-month schedule.	
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use
Dosage and administration details:	
Subjects received 1 dose 0.5 mL of saline at Month 2.	

Number of subjects in period 1	Group 1 rLP2086 Lot 1	Group 2 rLP2086 Lot 2	Group 3 rLP2086 Lot 3
Started	1508	598	587
Completed	1353	537	521
Not completed	155	61	66
Consent withdrawn by subject	33	14	10
Adverse Event	11	5	6
No longer meets eligibility criteria	11	2	3
Protocol deviation	10	5	6
Pregnancy	3	1	2
No longer willing to participate	32	13	12
Unspecified	7	1	4
Medication error without associated AE	1	-	-
Lost to follow-up	47	20	23

Number of subjects in period 1	Group 4 HAV/Saline
Started	897
Completed	815
Not completed	82
Consent withdrawn by subject	12
Adverse Event	3
No longer meets eligibility criteria	5
Protocol deviation	6
Pregnancy	1

No longer willing to participate	17
Unspecified	4
Medication error without associated AE	1
Lost to follow-up	33

Baseline characteristics

Reporting groups	
Reporting group title	Group 1 rLP2086 Lot 1
Reporting group description: Lot 1 on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 2 rLP2086 Lot 2
Reporting group description: Lot 2 on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 3 rLP2086 Lot 3
Reporting group description: Lot 3 on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 4 HAV/Saline
Reporting group description: Hepatitis A virus vaccine (HAV) on a 0- and 6-month schedule and saline at Month 2.	

Reporting group values	Group 1 rLP2086 Lot 1	Group 2 rLP2086 Lot 2	Group 3 rLP2086 Lot 3
Number of subjects	1508	598	587
Age categorical Units: Subjects			
2-11 years	356	136	135
12-17 years	995	389	382
18-64 years	157	73	70
Age Continuous | Units: years			
arithmetic mean	13.9	14	13.9
standard deviation	± 2.6	± 2.6	± 2.6
Gender, Male/Female Units: Participants			
Female	737	286	274
Male	771	312	313

Reporting group values	Group 4 HAV/Saline	Total	
Number of subjects	897	3590	
Age categorical Units: Subjects			
2-11 years	222	849	
12-17 years	580	2346	
18-64 years	95	395	
Age Continuous | Units: years			
arithmetic mean	13.9		
standard deviation	± 2.6	-	
Gender, Male/Female Units: Participants			
Female	443	1740	
Male	454	1850	

End points

End points reporting groups

Reporting group title	Group 1 rLP2086 Lot 1
Reporting group description: Lot 1 on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 2 rLP2086 Lot 2
Reporting group description: Lot 2 on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 3 rLP2086 Lot 3
Reporting group description: Lot 3 on a 0-, 2-, 6- month schedule.	
Reporting group title	Group 4 HAV/Saline
Reporting group description: Hepatitis A virus vaccine (HAV) on a 0- and 6-month schedule and saline at Month 2.	
Subject analysis set title	rLP2086 (Lots 1-3)
Subject analysis set type	Safety analysis
Subject analysis set description: Commercial lots 1, 2 and 3 on a 0-, 2-, 6-months schedule.	
Subject analysis set title	Group 4 HAV/Saline
Subject analysis set type	Safety analysis
Subject analysis set description: Hepatitis A virus vaccine (HAV) on a 0- and 6-month schedule and saline at Month 2.	

Primary: Percentage of Subjects with >=4 Fold Rise in Serum Bactericidal Assay Using Human Complement (hSBA) for 4 Primary Strains and Composite Response (hSBA >=Lower Limit of Quantification [LLOQ] for all 4 Primary Strains Combined)

End point title	Percentage of Subjects with >=4 Fold Rise in Serum Bactericidal Assay Using Human Complement (hSBA) for 4 Primary Strains and Composite Response (hSBA >=Lower Limit of Quantification [LLOQ] for all 4 Primary Strains Combined)[1][2]

End point description:

Evaluable immunogenicity population included all eligible subjects randomized, who received correct investigational product, had pre/post vaccination blood drawn at pre-specified time points, had valid and determinate assay results for proposed analysis, received no prohibited treatment or prohibited vaccines, and had no major protocol violations. Here, N signifies subjects with valid and determinate hSBA titers for given strain at specified time point.

End point type	Primary

End point timeframe:

One month after third bivalent rLP2086 vaccination

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.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1			
Subject group type	Reporting group			
Number of subjects analysed	1279			
Units: percentage of subjects				
number (confidence interval 95%)				
Composite hSBA response (N= 1170)	83.5 (81.3 to 85.6)			
PMB80[A22] (N= 1225)	83.2 (81 to 85.2)			
PMB2001[A56] (N= 1128)	90.2 (88.4 to 91.9)			
PMB2948[B24] (N= 1235)	79.8 (77.4 to 82)			
PMB2707[B44] (N= 1203)	85.9 (83.8 to 87.8)			

Statistical analyses

No statistical analyses for this end point

Primary: hSBA Geometric Mean Titers (GMTs) for Each of the 2 Primary Test Strains Measured 1 Month After the Third Vaccination with Bivalent rLP2086 Vaccine

End point title	hSBA Geometric Mean Titers (GMTs) for Each of the 2 Primary Test Strains Measured 1 Month After the Third Vaccination with Bivalent rLP2086 Vaccine [3]

End point description:

Evaluable immunogenicity population. Here N signifies subjects with valid and determinate hSBA titers for the given strain.

End point type	Primary

End point timeframe:

One month after third bivalent rLP2086 vaccination

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1	Group 2 rLP2086 Lot 2	Group 3 rLP2086 Lot 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1279	519	493	
Units: titer				
geometric mean (confidence interval 95%)				
PMB80[A22] (N= 1266, 518, 492)	86.8 (82.29 to 91.5)	84.3 (77.54 to 91.68)	85.1 (78.26 to 92.47)	
PMB2948[B24] (N= 1250, 516, 479)	24.1 (22.7 to 25.48)	25.3 (23.08 to 27.72)	25.2 (23.03 to 27.58)	

Statistical analyses

Statistical analysis title	PMB80[A22]:rLP2086 Lot 1 vs rLP2086 Lot 2
Statistical analysis description:	
PMB80 [A22]: The lot consistency criteria was achieved if the 95% CI for all pairwise GMRs between lots are within (0.5, 2), for the strain PMB80.	
Comparison groups	Group 1 rLP2086 Lot 1 v Group 2 rLP2086 Lot 2
Number of subjects included in analysis	1798
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Ratio of GMTs
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.14

Statistical analysis title	PMB80[A22]:rLP2086 Lot 1 vs rLP2086 Lot 3
Statistical analysis description:	
PMB80 [A22]: The lot consistency criteria was achieved if the 95% CI for all pairwise GMRs between lots are within (0.5, 2), for the strain PMB80.	
Comparison groups	Group 1 rLP2086 Lot 1 v Group 3 rLP2086 Lot 3
Number of subjects included in analysis	1772
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Ratio of GMTs
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.13

Statistical analysis title	PMB80[A22]: rLP2086 Lot 2 vs rLP2086 Lot 3
Statistical analysis description:	
PMB80 [A22]: The lot consistency criteria was achieved if the 95% CI for all pairwise GMRs between lots are within (0.5, 2), for the strain PMB80.	
Comparison groups	Group 2 rLP2086 Lot 2 v Group 3 rLP2086 Lot 3
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Ratio of GMTs
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.12

Statistical analysis title	PMB2948[B24]:rLP2086 Lot 1 vs rLP2086 Lot 2
Statistical analysis description:	
PMB2948 [B24]: The lot consistency criteria was achieved if the 95% CI for all pairwise GMRs between lots are within (0.5, 2), for the strain PMB2948.	
Comparison groups	Group 1 rLP2086 Lot 1 v Group 2 rLP2086 Lot 2
Number of subjects included in analysis	1798
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Ratio of GMTs
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.06

Statistical analysis title	PMB2948[B24]: rLP2086 Lot 1 vs rLP2086 Lot 3
Statistical analysis description:	
PMB2948 [B24]: The lot consistency criteria was achieved if the 95% CI for all pairwise GMRs between lots are within (0.5, 2), for the strain PMB2948.	
Comparison groups	Group 1 rLP2086 Lot 1 v Group 3 rLP2086 Lot 3
Number of subjects included in analysis	1772
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Ratio of GMTs
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.06

Statistical analysis title	PMB2948[B24]: rLP2086 Lot 2 vs rLP2086 Lot 3
Statistical analysis description:	
PMB2948 [B24]: The lot consistency criteria was achieved if the 95% CI for all pairwise GMRs between lots are within (0.5, 2), for the strain PMB2948	
Comparison groups	Group 2 rLP2086 Lot 2 v Group 3 rLP2086 Lot 3
Number of subjects included in analysis	1012
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Ratio of GMTs
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.14

Primary: Percentage of Subjects Reporting Local Reactions (LRs) Within 7 Days After First Vaccination

End point title	Percentage of Subjects Reporting Local Reactions (LRs) Within 7 Days After First Vaccination[4]

End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or HAV) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary

End point timeframe:

Within 7 days after first vaccination

Notes:

[4] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2681[5]	890[6]		
Units: percentage of participants				
number (confidence interval 95%)				
Pain at injection site: Any	86.7 (85.4 to 88)	47 (43.6 to 50.3)		
Pain at injection site: Mild	41.1 (39.2 to 43)	36.5 (33.3 to 39.8)		
Pain at injection site: Moderate	40.7 (38.8 to 42.5)	9.9 (8 to 12)		
Pain at injection site: Severe	5 (4.2 to 5.9)	0.6 (0.2 to 1.3)		
Redness: Any	16.2 (14.8 to 17.7)	1.3 (0.7 to 2.3)		
Redness: Mild	5.6 (4.7 to 6.5)	1.2 (0.6 to 2.2)		
Redness: Moderate	8.8 (7.7 to 9.9)	0.1 (0 to 0.6)		
Redness: Severe	1.9 (1.4 to 2.5)	0 (0 to 0.4)		
Swelling: Any	18 (16.5 to 19.5)	2.2 (1.4 to 3.4)		
Swelling: Mild	8.5 (7.4 to 9.6)	1.8 (1 to 2.9)		
Swelling: Moderate	8.8 (7.7 to 9.9)	0.4 (0.1 to 1.1)		
Swelling: Severe	0.7 (0.5 to 1.1)	0 (0 to 0.4)		

Notes:

[5] - Number of subjects analyzed signifies subjects with known values after the first vaccination.

[6] - Number of subjects analyzed signifies subjects with known values after the first vaccination.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Local Reactions (LRs) Within 7 Days After Second Vaccination

End point title	Percentage of Subjects Reporting Local Reactions (LRs) Within 7 Days After Second Vaccination[7]

End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary

End point timeframe:

Within 7 days after second vaccination

Notes:

[7] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2545[8]	843[9]		
Units: percentage of subjects				
number (confidence interval 95%)				
Pain at injection site: Any	77.7 (76 to 79.3)	15.2 (12.8 to 17.8)		
Pain at injection site: Mild	39.4 (37.5 to 41.3)	12.3 (10.2 to 14.7)		
Pain at injection site: Moderate	33.2 (31.4 to 35.1)	2.7 (1.7 to 4.1)		
Pain at injection site: Severe	5.1 (4.2 to 6)	0.1 (0 to 0.7)		
Redness: Any	12.5 (11.2 to 13.8)	0.6 (0.2 to 1.4)		
Redness: Mild	5.2 (4.4 to 6.2)	0.6 (0.2 to 1.4)		
Redness: Moderate	6.1 (5.2 to 7.1)	0 (0 to 0.4)		
Redness: Severe	1.1 (0.8 to 1.6)	0 (0 to 0.4)		
Swelling: Any	13.9 (12.5 to 15.3)	0.6 (0.2 to 1.4)		
Swelling: Mild	6.3 (5.4 to 7.3)	0.5 (0.1 to 1.2)		
Swelling: Moderate	7.3 (6.4 to 8.4)	0.1 (0 to 0.7)		
Swelling: Severe	0.2 (0.1 to 0.5)	0 (0 to 0.4)		

Notes:

[8] - Number of subjects analyzed signifies subjects with known values after the second vaccination.

[9] - Number of subjects analyzed signifies subjects with known values after the second vaccination.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Local Reactions (LRs) Within 7 Days After Third Vaccination

End point title	Percentage of Subjects Reporting Local Reactions (LRs) Within 7 Days After Third Vaccination[10]

End point description:

Safety population for third vaccination included all subjects who received third dose of investigational product (rLP2086 or HAV) and for whom safety information was available from third vaccination until post third-vaccination blood draw.

End point type	Primary

End point timeframe:

Within 7 days after third vaccination

Notes:

[10] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2421[11]	821[12]		
Units: percentage of participants				
number (confidence interval 95%)				
Pain at injection site: Any	76 (74.2 to 77.7)	34 (30.7 to 37.3)		
Pain at injection site: Mild	34.1 (32.2 to 36)	23.8 (20.9 to 26.8)		
Pain at injection site: Moderate	36.5 (34.6 to 38.5)	9.9 (7.9 to 12.1)		
Pain at injection site: Severe	5.4 (4.5 to 6.4)	0.4 (0.1 to 1.1)		
Redness: Any	13.9 (12.5 to 15.3)	1.1 (0.5 to 2.1)		
Redness: Mild	4.9 (4.1 to 5.8)	1 (0.4 to 1.9)		
Redness: Moderate	6.8 (5.8 to 7.9)	0.1 (0 to 0.7)		
Redness: Severe	2.2 (1.6 to 2.9)	0 (0 to 0.4)		
Swelling: Any	15.4 (14 to 16.9)	0.9 (0.3 to 1.7)		
Swelling: Mild	7.9 (6.8 to 9)	0.7 (0.3 to 1.6)		
Swelling: Moderate	6.8 (5.8 to 7.9)	0.1 (0 to 0.7)		
Swelling: Severe	0.7 (0.4 to 1.1)	0 (0 to 0.4)		

Notes:

[11] - Number of subjects analyzed signifies subjects with known values after third vaccination.

[12] - Number of subjects analyzed signifies subjects with known values after third vaccination.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After First Vaccination

End point title	Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After First Vaccination[13]

End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or HAV) and for whom safety information was available from first vaccination until prior to second vaccination. N signifies subjects with known values reporting specific characteristic.

End point type	Primary

End point timeframe:

Within 7 days after first vaccination

Notes:

[13] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2681[14]	890[15]		
Units: percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C(N=2679, 890)	6.4 (5.5 to 7.4)	1.9 (1.1 to 3)		
Fever 38 to <38.5degreesC(N=2679, 890)	4 (3.3 to 4.8)	1.3 (0.7 to 2.3)		
Fever 38.5 to<39degreesC(N=2679, 890)	1.9 (1.5 to 2.5)	0.3 (0.1 to 1)		
Fever 39 to 40degreesC(N=2679, 890)	0.5 (0.3 to 0.8)	0.2 (0 to 0.8)		
Fever >40 degreesC(N=2679, 890)	0 (0 to 0.1)	0 (0 to 0.4)		
Vomiting:Any(N=2681,890)	3.7 (3 to 4.5)	1.9 (1.1 to 3)		
Vomiting:Mild(N=2681,890)	2.8 (2.2 to 3.5)	1.7 (0.9 to 2.8)		
Vomiting:Moderate(N=2681,890)	0.9 (0.6 to 1.4)	0.2 (0 to 0.8)		
Vomiting:Severe(N=2681,890)	0 (0 to 0.1)	0 (0 to 0.4)		
Diarrhea:Any(N=2681,890)	10.6 (9.5 to 11.9)	12.1 (10.1 to 14.5)		
Diarrhea:Mild(N=2681,890)	9.1 (8 to 10.3)	10.9 (8.9 to 13.1)		
Diarrhea:Moderate(N=2681,890)	1.3 (0.9 to 1.8)	1.1 (0.5 to 2.1)		
Diarrhea:Severe(N=2681,890)	0.3 (0.1 to 0.5)	0.1 (0 to 0.6)		
Headache:Any(N=2681,890)	51.8 (49.9 to 53.8)	37.2 (34 to 40.5)		
Headache:Mild(N=2681,890)	28.7 (27 to 30.5)	24 (21.3 to 27)		
Headache:Moderate(N=2681,890)	21 (19.4 to 22.6)	12.5 (10.4 to 14.8)		
Headache:Severe(N=2681,890)	2.2 (1.6 to 2.8)	0.7 (0.2 to 1.5)		
Fatigue:Any(N=2681,890)	54 (52.1 to 55.9)	40.3 (37.1 to 43.6)		
Fatigue:Mild(N=2681,890)	27.8 (26.1 to 29.5)	23.5 (20.7 to 26.4)		
Fatigue:Moderate(N=2681,890)	23.2 (21.6 to 24.8)	15.2 (12.9 to 17.7)		
Fatigue:Severe(N=2681,890)	3 (2.4 to 3.7)	1.7 (0.9 to 2.8)		
Chills:Any(N=2681,890)	25.3 (23.7 to 27)	17.2 (14.8 to 19.8)		
Chills:Mild(N=2681,890)	16.2 (14.8 to 17.6)	13.3 (11.1 to 15.7)		
Chills:Moderate(N=2681,890)	8 (7 to 9.1)	3.5 (2.4 to 4.9)		
Chills:Severe(N=2681,890)	1.2 (0.8 to 1.7)	0.4 (0.1 to 1.1)		
Muscle pain:Any(N=2681,890)	24.4 (22.8 to 26.1)	19.2 (16.7 to 22)		
Muscle pain:Mild(N=2681,890)	13.2 (11.9 to 14.5)	13.5 (11.3 to 15.9)		
Muscle pain:Moderate(N=2681,890)	10.1 (9 to 11.3)	5.4 (4 to 7.1)		
Muscle pain:Severe(N=2681,890)	1.2 (0.8 to 1.6)	0.3 (0.1 to 1)		
Joint pain:Any(N=2681,890)	21.9 (20.4 to 23.5)	13.6 (11.4 to 16)		
Joint pain:Mild(N=2681,890)	11.8 (10.6 to 13.1)	8.3 (6.6 to 10.3)		
Joint pain:Moderate(N=2681,890)	8.7 (7.7 to 9.8)	4.6 (3.3 to 6.2)		
Joint pain:Severe(N=2681,890)	1.4 (1 to 1.9)	0.7 (0.2 to 1.5)		
Antipyretic medication(N=2681,890)	20.7 (19.2 to 22.3)	10.4 (8.5 to 12.6)		

Notes:

[14] - Number of subjects analyzed signifies subjects with known values after the first vaccination.

[15] - Number of subjects analyzed signifies subjects with known values after the first vaccination.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After Second Vaccination

End point title	Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After Second Vaccination[16]

End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination. N signifies subjects with known values reporting specific characteristic.

End point type	Primary

End point timeframe:

Within 7 days after second vaccination

Notes:

[16] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2545[17]	843[18]		
Units: percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C(N=2540, 840)	2 (1.5 to 2.6)	1.5 (0.8 to 2.6)		
Fever 38 to <38.5 degreesC(N=2540, 840)	1.2 (0.8 to 1.7)	0.7 (0.3 to 1.5)		
Fever 38.5 to<39 degrees C(N=2540, 840)	0.7 (0.4 to 1.1)	0.7 (0.3 to 1.5)		
Fever 39 to 40 degrees C(N=2540, 840)	0.1 (0 to 0.3)	0.1 (0 to 0.7)		
Fever >40 degrees C(N=2540, 840)	0 (0 to 0.1)	0 (0 to 0.4)		
Vomiting:Any(N=2545, 843)	2.2 (1.6 to 2.8)	1.4 (0.7 to 2.5)		
Vomiting:Mild(N=2545, 843)	1.7 (1.3 to 2.3)	1.1 (0.5 to 2)		
Vomiting:Moderate(N=2545, 843)	0.4 (0.2 to 0.8)	0.4 (0.1 to 1)		
Vomiting:Severe(N=2545, 843)	0 (0 to 0.1)	0 (0 to 0.4)		
Diarrhea:Any(N=2545, 843)	7.6 (6.6 to 8.7)	9.1 (7.3 to 11.3)		
Diarrhea:Mild(N=2545, 843)	6.2 (5.3 to 7.2)	7.6 (5.9 to 9.6)		
Diarrhea:Moderate(N=2545, 843)	1.3 (0.9 to 1.8)	1.2 (0.6 to 2.2)		
Diarrhea:Severe(N=2545, 843)	0.1 (0 to 0.3)	0.4 (0.1 to 1)		
Headache:Any(N=2545, 843)	37.8 (35.9 to 39.8)	28.1 (25.1 to 31.3)		
Headache:Mild(N=2545, 843)	20.2 (18.7 to 21.8)	15.7 (13.3 to 18.3)		
Headache:Moderate(N=2545, 843)	16 (14.6 to 17.5)	10.9 (8.9 to 13.2)		

Headache:Severe(N=2545, 843)	1.7 (1.2 to 2.2)	1.5 (0.8 to 2.6)		
Fatigue:Any(N=2545, 843)	38.3 (36.4 to 40.2)	26.3 (23.4 to 29.4)		
Fatigue:Mild(N=2545, 843)	20.6 (19 to 22.2)	13.2 (11 to 15.6)		
Fatigue:Moderate(N=2545, 843)	15.8 (14.4 to 17.3)	11.7 (9.6 to 14.1)		
Fatigue:Severe(N=2545, 843)	1.9 (1.4 to 2.5)	1.4 (0.7 to 2.5)		
Chills:Any(N=2545, 843)	16 (14.6 to 17.4)	10.3 (8.3 to 12.6)		
Chills:Mild(N=2545, 843)	10.6 (9.4 to 11.9)	8.1 (6.3 to 10.1)		
Chills:Moderate(N=2545, 843)	4.8 (4 to 5.7)	1.8 (1 to 2.9)		
Chills:Severe(N=2545, 843)	0.6 (0.3 to 1)	0.5 (0.1 to 1.2)		
Muscle pain:Any(N=2545, 843)	17.8 (16.3 to 19.3)	10.3 (8.3 to 12.6)		
Muscle pain:Mild(N=2545, 843)	8.7 (7.6 to 9.8)	5.2 (3.8 to 6.9)		
Muscle pain:Moderate(N=2545, 843)	7.9 (6.8 to 9)	4.5 (3.2 to 6.1)		
Muscle pain:Severe(N=2545, 843)	1.2 (0.8 to 1.7)	0.6 (0.2 to 1.4)		
Joint pain:Any(N=2545, 843)	16.7 (15.3 to 18.2)	9.1 (7.3 to 11.3)		
Joint pain:Mild(N=2545, 843)	8.4 (7.4 to 9.6)	5 (3.6 to 6.7)		
Joint pain:Moderate(N=2545, 843)	7.5 (6.5 to 8.6)	3.4 (2.3 to 4.9)		
Joint pain:Severe(N=2545, 843)	0.8 (0.5 to 1.2)	0.7 (0.3 to 1.5)		
Antipyretic medication(N=2545, 843)	13.6 (12.3 to 15)	8.9 (7.1 to 11)		

Notes:

[17] - Number of subjects analyzed signifies subjects with known values after second vaccination.

[18] - Number of subjects analyzed signifies subjects with known values after second vaccination.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After Third Vaccination

End point title	Percentage of Subjects Reporting Systemic Events (SEs) and Antipyretic Use Within 7 Days After Third Vaccination[19]

End point description:

Safety population for third vaccination included all subjects who received third dose of investigational product (rLP2086 or HAV) and for whom safety information was available from third vaccination until post third-vaccination blood draw. N signifies subjects with known values reporting specific characteristic.

End point type	Primary

End point timeframe:

Within 7 days after third vaccination

Notes:

[19] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2421[20]	821[21]		
Units: percentage of subjects				
number (confidence interval 95%)				
Fever >=38 degrees C(N=2414, 819)	2.7 (2.1 to 3.4)	2.3 (1.4 to 3.6)		
Fever 38 to <38.5degreesC(N=2414, 819)	1.8 (1.3 to 2.4)	1.3 (0.7 to 2.4)		
Fever 38.5 to<39 degrees C(N=2414, 819)	0.6 (0.3 to 1)	0.4 (0.1 to 1.1)		
Fever 39 to 40 degrees C(N=2414, 819)	0.3 (0.1 to 0.6)	0.5 (0.1 to 1.2)		
Fever >40 degrees C(N=2414, 819)	0 (0 to 0.2)	0.1 (0 to 0.7)		
Vomiting:Any(N=2421, 821)	1.7 (1.3 to 2.3)	2.2 (1.3 to 3.4)		
Vomiting:Mild(N=2421, 821)	1.4 (1 to 2)	1.7 (0.9 to 2.8)		
Vomiting:Moderate(N=2421, 821)	0.3 (0.1 to 0.6)	0.5 (0.1 to 1.2)		
Vomiting:Severe(N=2421, 821)	0 (0 to 0.2)	0 (0 to 0.4)		
Diarrhea:Any(N=2421, 821)	7.7 (6.7 to 8.9)	7.6 (5.8 to 9.6)		
Diarrhea:Mild(N=2421, 821)	6.4 (5.5 to 7.5)	6.2 (4.7 to 8.1)		
Diarrhea:Moderate(N=2421, 821)	1 (0.6 to 1.5)	1.1 (0.5 to 2.1)		
Diarrhea:Severe(N=2421, 821)	0.3 (0.1 to 0.6)	0.2 (0 to 0.9)		
Headache:Any(N=2421, 821)	35.4 (33.5 to 37.4)	24.8 (21.9 to 28)		
Headache:Mild(N=2421, 821)	18.9 (17.3 to 20.5)	13.5 (11.3 to 16.1)		
Headache:Moderate(N=2421, 821)	15.2 (13.8 to 16.7)	10.4 (8.4 to 12.6)		
Headache:Severe(N=2421, 821)	1.3 (0.9 to 1.9)	1 (0.4 to 1.9)		
Fatigue:Any(N=2421, 821)	35.9 (34 to 37.9)	24.4 (21.5 to 27.4)		
Fatigue:Mild(N=2421, 821)	18.4 (16.9 to 20)	13.5 (11.3 to 16.1)		
Fatigue:Moderate(N=2421, 821)	15.2 (13.8 to 16.7)	10 (8 to 12.2)		
Fatigue:Severe(N=2421, 821)	2.3 (1.8 to 3)	0.9 (0.3 to 1.7)		
Chills:Any(N=2421, 821)	13.1 (11.7 to 14.5)	8.3 (6.5 to 10.4)		
Chills:Mild(N=2421, 821)	8.7 (7.6 to 9.9)	6.5 (4.9 to 8.4)		
Chills:Moderate(N=2421, 821)	3.8 (3.1 to 4.7)	1.7 (0.9 to 2.8)		
Chills:Severe(N=2421, 821)	0.5 (0.3 to 0.9)	0.1 (0 to 0.7)		
Muscle pain:Any(N=2421, 821)	17.6 (16.1 to 19.1)	11.1 (9 to 13.4)		
Muscle pain:Mild(N=2421, 821)	9.5 (8.4 to 10.8)	6.6 (5 to 8.5)		
Muscle pain:Moderate(N=2421, 821)	7.2 (6.2 to 8.3)	4.3 (3 to 5.9)		
Muscle pain:Severe(N=2421, 821)	0.8 (0.5 to 1.3)	0.2 (0 to 0.9)		
Joint pain:Any(N=2421, 821)	16 (14.6 to 17.5)	8.9 (7 to 11.1)		
Joint pain:Mild(N=2421, 821)	8.9 (7.8 to 10.1)	5.5 (4 to 7.3)		
Joint pain:Moderate(N=2421, 821)	5.9 (5 to 6.9)	3 (2 to 4.5)		
Joint pain:Severe(N=2421, 821)	1.2 (0.8 to 1.8)	0.4 (0.1 to 1.1)		
Antipyretic medication(N=2421, 821)	12.7 (11.4 to 14.1)	6.8 (5.2 to 8.8)		

Notes:

[20] - Number of subjects analyzed signifies subjects with known values after third vaccination.

[21] - Number of subjects analyzed signifies subjects with known values after third vaccination.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After First Vaccination

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After First Vaccination[22]

End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or HAV) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary

End point timeframe:

Within 30 days after first vaccination

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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	0.26 (0.1 to 0.5)	0.33 (0.1 to 1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Second Vaccination

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Second Vaccination[23]

End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary

End point timeframe:

Within 30 days after second vaccination

Notes:

[23] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2570	860		
Units: percentage of subjects				
number (confidence interval 95%)	0.23 (0.1 to 0.5)	0.23 (0 to 0.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Third Vaccination

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After Third Vaccination[24]

End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product (rLP2086 or HAV) and for whom safety information was available from third vaccination until post third-vaccination blood draw.

End point type	Primary

End point timeframe:

Within 30 days after third vaccination

Notes:

[24] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2462	835		
Units: percentage of subjects				
number (confidence interval 95%)	0.32 (0.1 to 0.6)	0.36 (0.1 to 1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After any Vaccination

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Within 30 Days After any Vaccination[25]

End point description:

Safety population included all the 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:

[25] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	0.78 (0.5 to 1.2)	0.89 (0.4 to 1.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) During the Vaccination Phase

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) During the Vaccination Phase[26]

End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/s aline) and had safety data available.

End point type	Primary

End point timeframe:

From the first vaccination up to 1 month after the third vaccination

Notes:

[26] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	1.49 (1.1 to 2)	1.9 (1.1 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) During the Follow-up Phase

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) During the Follow-up Phase[27]

End point description:

Safety population: all subjects who had at least 1 dose investigational product (rLP2086 or HAV/saline) for whom safety information was available from after post third-vaccination blood draw to 6 months after last study vaccination.

End point type	Primary

End point timeframe:

From 1 month after third vaccination up to 6 months after the third vaccination

Notes:

[27] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2524	839		
Units: percentage of subjects				
number (confidence interval 95%)	0.44 (0.2 to 0.8)	0.6 (0.2 to 1.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Throughout the Study Period

End point title	Percentage of Subjects With at Least 1 Serious Adverse Event (SAE) Throughout the Study Period[28]

End point description:

Safety population included all the 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 first vaccination up to 6 month after the third vaccination

Notes:

[28] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	1.89 (1.4 to 2.5)	2.45 (1.5 to 3.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After First Vaccination

End point title	Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After First Vaccination[29]

End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or HAV) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary

End point timeframe:

Within 30 days after first vaccination

Notes:

[29] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	5.27 (4.5 to 6.2)	6.69 (5.1 to 8.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After Second Vaccination

End point title	Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After Second Vaccination[30]

End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary

End point timeframe:

Within 30 days after second vaccination

Notes:

[30] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2570	860		
Units: percentage of subjects				
number (confidence interval 95%)	5.91 (5 to 6.9)	6.51 (5 to 8.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After Third Vaccination

End point title	Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After Third Vaccination[31]

End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product (rLP2086 or HAV) and for whom safety information was available from third vaccination until post third-vaccination blood draw.

End point type	Primary

End point timeframe:

Within 30 days after third vaccination

Notes:

[31] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2462	835		
Units: percentage of subjects				
number (confidence interval 95%)	5.81 (4.9 to 6.8)	7.43 (5.7 to 9.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After any Vaccination

End point title	Percentage of Subjects With at Least 1 Medically Attended AE Within 30 Days After any Vaccination[32]

End point description:

Safety population included all the 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:

[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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	14.18 (12.9 to 15.6)	16.61 (14.2 to 19.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE During the Vaccination Phase

End point title	Percentage of Subjects With at Least 1 Medically Attended AE During the Vaccination Phase[33]

End point description:

Safety population included all the 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 first vaccination up to 1 month after the third vaccination

Notes:

[33] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	25.29 (23.7 to 27)	27.87 (25 to 30.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE During the Follow-Up Phase

End point title	Percentage of Subjects With at Least 1 Medically Attended AE During the Follow-Up Phase[34]

End point description:

Safety population: all subjects who had at least 1 dose of investigational product (rLP2086 or HAV/saline) for whom safety information was available from after post-vaccination 3 blood draw to 6 months after last study vaccination.

End point type	Primary

End point timeframe:

From 1 month after third vaccination up to 6 months after the third vaccination

Notes:

[34] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2524	839		
Units: percentage of subjects				
number (confidence interval 95%)	15.61 (14.2 to 17.1)	16.92 (14.4 to 19.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Medically Attended AE Throughout the Study Period

End point title	Percentage of Subjects With at Least 1 Medically Attended AE Throughout the Study Period[35]

End point description:

Safety population included all the 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 first vaccination up to 6 month after the third vaccination

Notes:

[35] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	32.38 (30.6 to 34.2)	35.56 (32.4 to 38.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After First Vaccination

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After First Vaccination[36]

End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or HAV) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary

End point timeframe:

Within 30 days after first vaccination

Notes:

[36] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	0 (0 to 0.1)	0.11 (0 to 0.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After Second Vaccination

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After Second Vaccination[37]

End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or saline) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary

End point timeframe:

30 days after second vaccination

Notes:

[37] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2570	860		
Units: percentage of subjects				
number (confidence interval 95%)	0.08 (0 to 0.3)	0.12 (0 to 0.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After Third Vaccination

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After Third Vaccination[38]

End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product(rLP2086 or HAV)and for whom safety information was available from third vaccination until post third-vaccination blood draw.

End point type	Primary

End point timeframe:

Within 30 days after third vaccination

Notes:

[38] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2462	835		
Units: percentage of subjects				
number (confidence interval 95%)	0.12 (0 to 0.4)	0 (0 to 0.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After any Vaccination

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Within 30 Days After any Vaccination[39]

End point description:

Safety population included all the 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:

[39] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	0.19 (0.1 to 0.4)	0.22 (0 to 0.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition During the Vaccination Phase

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition During the Vaccination Phase[40]

End point description:

Safety population included all the 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 first vaccination up to 1 month after the third vaccination

Notes:

[40] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	0.37 (0.2 to 0.7)	0.56 (0.2 to 1.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition During the Follow-Up Phase

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition During the Follow-Up Phase[41]

End point description:

Safety population: all subjects who had at least 1 dose of investigational product (rLP2086 or

HAV/saline) for whom safety information was available from after post third-vaccination blood draw to 6 months after last study vaccination.

End point type	Primary

End point timeframe:

From 1 month after third vaccination up to 6 months after the third vaccination

Notes:

[41] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2524	839		
Units: percentage of subjects				
number (confidence interval 95%)	0.2 (0.1 to 0.5)	0.6 (0.2 to 1.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Throughout the Study Period

End point title	Percentage of Subjects With at Least 1 Newly Diagnosed Chronic Medical Condition Throughout the Study Period[42]

End point description:

Safety population included all subjects who received at least 1 dose of the investigational product and had safety information available.

End point type	Primary

End point timeframe:

From the first vaccination up to 6 month after the third vaccination

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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	0.56 (0.3 to 0.9)	1.11 (0.5 to 2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE) WIthin 30 Days After First Vaccination

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE) WIthin 30 Days After First Vaccination[43]

End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or HAV) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary

End point timeframe:

Within 30 days after first vaccination

Notes:

[43] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	9.51 (8.4 to 10.7)	10.7 (8.8 to 12.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Second Vaccination

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Second Vaccination[44]

End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or HAV) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary

End point timeframe:

Within 30 days after second vaccination

Notes:

[44] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2570	860		
Units: percentage of subjects				
number (confidence interval 95%)	11.48 (10.3 to 12.8)	12.67 (10.5 to 15.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Third Vaccination

End point title	Percentage of Subjects With at Least 1 Adverse Event (AE) Within 30 Days After Third Vaccination[45]

End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product (rLP2086 or HAV) and for whom safety information was available from third vaccination until post third-vaccination blood draw.

End point type	Primary

End point timeframe:

Within 30 days after third vaccination

Notes:

[45] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2462	835		
Units: percentage of subjects				
number (confidence interval 95%)	9.91 (8.8 to 11.2)	10.78 (8.8 to 13.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event Within 30 Days After any Vaccination

End point title	Percentage of Subjects With at Least 1 Adverse Event Within 30 Days After any Vaccination[46]

End point description:

Safety population included all the 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:

[46] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	25.32 (23.7 to 27)	26.76 (23.9 to 29.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With at Least 1 Adverse Event During the Vaccination Phase

End point title	Percentage of Subjects With at Least 1 Adverse Event During the Vaccination Phase[47]

End point description:

Safety population included all the 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 first vaccination up to 1 month after the third vaccination

Notes:

[47] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	40.74 (38.9 to 42.6)	43.7 (40.4 to 47)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting at Least 1 Immediate AE After First Vaccination

End point title	Percentage of Subjects Reporting at Least 1 Immediate AE After First Vaccination[48]

End point description:

Safety population for first vaccination included all subjects who received the first dose of investigational product (rLP2086 or HAV) and for whom safety information was available from first vaccination until prior to second vaccination.

End point type	Primary

End point timeframe:

Within 30 minutes after first vaccination

Notes:

[48] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2693	897		
Units: percentage of subjects				
number (confidence interval 95%)	0.1 (0 to 0.4)	0.2 (0 to 0.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting at Least 1 Immediate AE After Second Vaccination

End point title	Percentage of Subjects Reporting at Least 1 Immediate AE After Second Vaccination[49]

End point description:

Safety population for second vaccination included all subjects who received the second dose of investigational product (rLP2086 or HAV) and for whom safety information was available from second vaccination until prior to third vaccination.

End point type	Primary

End point timeframe:

Within 30 minutes after second vaccination

Notes:

[49] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2570	860		
Units: percentage of subjects				
number (confidence interval 95%)	0.2 (0 to 0.4)	0.1 (0 to 0.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting at Least 1 Immediate AE After Third Vaccination

End point title	Percentage of Subjects Reporting at Least 1 Immediate AE After Third Vaccination[50]

End point description:

Safety population for third vaccination included all subjects who received the third dose of investigational product (rLP2086 or HAV) and for whom safety information was available from third

vaccination until post third-vaccination blood draw.

End point type	Primary

End point timeframe:

Within 30 minutes after third vaccination

Notes:

[50] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2462	835		
Units: percentage of subjects				
number (confidence interval 95%)	0.1 (0 to 0.3)	0 (0 to 0.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Days Subjects Missed School or Work due to AE During the Vaccination Phase

End point title	Number of Days Subjects Missed School or Work due to AE During the Vaccination Phase[51]

End point description:

Safety population included all the subjects who received at least 1 dose of the investigational product (rLP2086 or HAV/s aline) and had safety data available.

End point type	Primary

End point timeframe:

From the first vaccination up to 1 month after the third vaccination

Notes:

[51] - 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	rLP2086 (Lots 1-3)	Group 4 HAV/Saline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	539	195		
Units: days				
arithmetic mean (standard deviation)	3.9 (± 6.56)	4 (± 5.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titers >=LLOQ for 10 Secondary Strains Before First Vaccination and 1 Month After Third Bivalent rLP2086 Vaccination

End point title	Percentage of Subjects With hSBA Titers >=LLOQ for 10 Secondary Strains Before First Vaccination and 1 Month After Third Bivalent rLP2086 Vaccination[52]

End point description:

Evaluable immunogenicity population. Here, N signifies subjects with valid and determinate hSBA titers for the given strain at the specified time point.

End point type	Secondary

End point timeframe:

Before first vaccination, 1 month after third vaccination

Notes:

[52] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1			
Subject group type	Reporting group			
Number of subjects analysed	300[53]			
Units: percentage of subjects				
number (confidence interval 95%)				
PMB3175[A29]:Before Vaccination1(N= 269)	17.5 (13.1 to 22.5)			
PMB3175[A29]:1Month after Vaccination3(N= 278)	98.6 (96.4 to 99.6)			
PMB3010[A06]:Before Vaccination1(N= 277)	9.4 (6.2 to 13.5)			
PMB3010[A06]:1Month after Vaccination3(N= 280)	95.7 (92.6 to 97.8)			
PMB3040[A07]:Before Vaccination1(N= 269)	43.1 (37.1 to 49.3)			
PMB3040[A07]:1Month after Vaccination3(N= 280)	96.4 (93.5 to 98.3)			
PMB824[A12]:Before Vaccination1(N= 280)	3.9 (2 to 6.9)			
PMB824[A12]:1Month after Vaccination3(N= 277)	75.1 (69.6 to 80.1)			
PMB1672[A15]:Before Vaccination1(N= 270)	20.7 (16.1 to 26.1)			
PMB1672[A15]:1Month after Vaccination3(N= 266)	87.2 (82.6 to 91)			
PMB1989[A19]:Before Vaccination1(N= 274)	11.3 (7.8 to 15.7)			
PMB1989[A19]:1Month after Vaccination3(N= 275)	92.7 (89 to 95.5)			
PMB1256[B03]:Before Vaccination1 (N= 280)	4.3 (2.2 to 7.4)			
PMB1256[B03]:1Month after Vaccination3(N= 279)	92.5 (88.7 to 95.3)			
PMB866[B09]:Before Vaccination1(N= 277)	15.2 (11.2 to 19.9)			
PMB866[B09]:1Month after Vaccination3(N= 276)	86.2 (81.6 to 90.1)			
PMB431[B15]:Before Vaccination1(N= 275)	28.7 (23.5 to 34.5)			
PMB431[B15]:1Month after Vaccination3(N= 281)	98.2 (95.9 to 99.4)			
PMB648[B16]:Before Vaccination1(N= 276)	7.6 (4.8 to 11.4)			

PMB648[B16]:1Month after Vaccination3(N= 278)	81.7 (76.6 to 86)			

Notes:

[53] - Number of subjects analyzed signifies subjects with valid, determinate hSBA titers for given strain

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titers >=1:4, >=1:8, >=1:16, >=1:32, >=1:64, >=1:128 for Each of the 10 Secondary Strains, Before Vaccination 1 and 1 Month After the Third Bivalent rLP2086 Vaccination

End point title	Percentage of Subjects With hSBA Titers >=1:4, >=1:8, >=1:16, >=1:32, >=1:64, >=1:128 for Each of the 10 Secondary Strains, Before Vaccination 1 and 1 Month After the Third Bivalent rLP2086 Vaccination [54]

End point description:

Evaluable immunogenicity population. Here, N signifies subjects with valid and determinate hSBA titers for the given strain at the specified time point.

End point type	Secondary

End point timeframe:

Before first vaccination, 1 month after third vaccination (Vac)

Notes:

[54] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1			
Subject group type	Reporting group			
Number of subjects analysed	300[55]			
Units: percentage of subjects				
number (confidence interval 95%)				
Before Vaccination1:PMB3175[A29]1:4(N=269)	19 (14.5 to 24.2)			
1 month after Vac3:PMB3175[A29]1:4(N=278)	98.6 (96.4 to 99.6)			
Before Vaccination1:PMB3175[A29]1:8(N=269)	17.5 (13.1 to 22.5)			
1 month after Vac3:PMB3175[A29]1:8(N=278)	98.6 (96.4 to 99.6)			
Before Vaccination 1:PMB3175[A29]1:16(N=269)	16.7 (12.5 to 21.7)			
1 month after Vac3:PMB3175[A29]1:16(N=278)	98.6 (96.4 to 99.6)			
Before Vaccination1:PMB3175[A29]1:32(N=26	10.8 (7.3 to 15.1)			
1 month after Vac3:PMB3175[A29]1:32(N=278)	97.5 (94.9 to 99)			
Before Vaccination 1:PMB3175[A29]1:64(N=269)	4.8 (2.6 to 8.1)			
1 month after Vac3:PMB3175[A29]1:64(N=278)	86 (81.3 to 89.8)			
Before Vaccination 1:PMB3175[A29]1:128(N=269)	1.1 (0.2 to 3.2)			

1 month after Vac3:PMB3175[A29]1:128(N=278)	52.2 (46.1 to 58.2)			
Before Vaccination 1:PMB3010[A06]1:4(N=277)	9.7 (6.5 to 13.9)			
1 month after Vac3:PMB3010[A06]1:4(N=280)	96.1 (93.1 to 98)			
Before Vaccination 1:PMB3010[A06]1:8(N=277)	9.7 (6.5 to 13.9)			
1 month after Vac3:PMB3010[A06]1:8(N=280)	96.1 (93.1 to 98)			
Before Vaccination 1:PMB3010[A06]1:16(N=277)	9.4 (6.2 to 13.5)			
1 month after Vac3:PMB3010[A06]1:16(N=280)	95.7 (92.6 to 97.8)			
Before Vaccination 1:PMB3010[A06]1:32(N=277)	6.1 (3.6 to 9.6)			
1 month after Vac3:PMB3010[A06]1:32(N=280)	93.6 (90 to 96.1)			
Before Vaccination1: PMB3010[A06]1:64(N=277)	2.9 (1.3 to 5.6)			
1 month after Vac3:PMB3010[A06]1:64(N=280)	78.2 (72.9 to 82.9)			
Before Vaccination1:PMB3010[A06]1:128(N=2	1.4 (0.4 to 3.7)			
1 month after Vac3:PMB3010[A06]1:128(N=280)	44.3 (38.4 to 50.3)			
Before Vaccination1:PMB3040[A07]1:4(N=269)	43.1 (37.1 to 49.3)			
1 month after Vac3:PMB3040[A07]1:4(N=280)	96.4 (93.5 to 98.3)			
Before Vaccination1:PMB3040[A07]1:8(N=269)	43.1 (37.1 to 49.3)			
1 month after Vac3:PMB3040[A07]1:8(N=280)	96.4 (93.5 to 98.3)			
Before Vaccination1:PMB3040[A07]1:16(N=26	42.8 (36.8 to 48.9)			
1 month after Vac3:PMB3040[A07]1:16(N=280)	96.4 (93.5 to 98.3)			
Before Vaccination1:PMB3040[A07]1:32(N=26	37.2 (31.4 to 43.3)			
1 month after Vac3:PMB3040[A07]1:32(N=280)	93.6 (90 to 96.1)			
Before Vaccination1:PMB3040[A07]1:64(N=26	21.6 (16.8 to 27)			
1 month after Vac3:PMB3040[A07]1:64(N=280)	78.2 (72.9 to 82.9)			
Before Vaccination1:PMB3040[A07]1:128(N=2	5.6 (3.2 to 9)			
1 month after Vac3:PMB3040[A07]1:128(N=280)	30.4 (25 to 36.1)			
Before Vaccination1:PMB824[A12]1:4(N=280)	5.4 (3 to 8.7)			
1 month after Vac3:PMB824[A12]1:4(N=277)	77.6 (72.2 to 82.4)			
Before Vaccination1:PMB824[A12]1:8(N=280)	4.6 (2.5 to 7.8)			
1 month after Vac3:PMB824[A12]1:8(N=277)	77.3 (71.9 to 82.1)			
Before Vaccination1:PMB824[A12]1:16(N=280)	3.9 (2 to 6.9)			
1 month after Vac3:PMB824[A12]1:16(N=277)	75.1 (69.6 to 80.1)			

Before Vaccination1:PMB824[A12]1:32(N=280)	2.5 (1 to 5.1)			
1 month after Vac3:PMB824[A12]1:32(N=277)	51.3 (45.2 to 57.3)			
Before Vaccination1:PMB824[A12]1:64(N=280)	0 (0 to 1.3)			
1 month after Vac3:PMB824[A12]1:64(N=277)	19.5 (15 to 24.7)			
Before Vaccination1:PMB824[A12]1:128(N=28	0 (0 to 1.3)			
1 month after Vac3:PMB824[A12]1:128(N=277)	1.8 (0.6 to 4.2)			
Before Vaccination1:PMB1672[A15]1:4(N=270)	22.6 (17.7 to 28.1)			
1 month after Vac3:PMB1672[A15]1:4(N=266)	87.2 (82.6 to 91)			
Before Vaccination1:PMB1672[A15]1:8(N=270)	20.7 (16.1 to 26.1)			
1 month after Vac3:PMB1672[A15]1:8(N=266)	87.2 (82.6 to 91)			
Before Vaccination1:PMB1672[A15]1:16(N=27	17 (12.8 to 22.1)			
1 month after Vac3:PMB1672[A15]1:16(N=266)	85 (80.1 to 89)			
Before Vaccination1:PMB1672[A15]1:32(N=27	13.3 (9.5 to 18)			
1 month after Vac3:PMB1672[A15]1:32(N=266)	71.4 (65.6 to 76.8)			
Before Vaccination1:PMB1672[A15]1:64(N=27	3.7 (1.8 to 6.7)			
1 month after Vac3:PMB1672[A15]1:64(N=266)	40.2 (34.3 to 46.4)			
Before Vaccination1:PMB1672[A15]1:128(N=2	0.4 (0 to 2)			
1 month after Vac3:PMB1672[A15]1:128(N=266)	10.5 (7.1 to 14.9)			
Before Vaccination1:PMB1989[A19]1:4(N=274)	20.8 (16.2 to 26.1)			
1 month after Vac3:PMB1989[A19]1:4(N=275)	93.8 (90.3 to 96.4)			
Before Vaccination1:PMB1989[A19]1:8(N=274)	18.6 (14.2 to 23.7)			
1 month after Vac3:PMB1989[A19]1:8(N=275)	93.8 (90.3 to 96.4)			
Before Vaccination1:PMB1989[A19]1:16(N=27	11.3 (7.8 to 15.7)			
1 month after Vac3:PMB1989[A19]1:16(N=275)	92.7 (89 to 95.5)			
Before Vaccination1:PMB1989[A19]1:32(N=27	5.8 (3.4 to 9.3)			
1 month after Vac3:PMB1989[A19]1:32(N=275)	85.5 (80.7 to 89.4)			
Before Vaccination1:PMB1989[A19]1:64(N=27	1.8 (0.6 to 4.2)			
1 month after Vac3:PMB1989[A19]1:64(N=275)	60 (53.9 to 65.8)			
Before Vaccination1:PMB1989[A19]1:128(N=2	0.4 (0 to 2)			
1 month after Vac3:PMB1989[A19]1:128(N=275)	33.1 (27.6 to 39)			
Before Vaccination1:PMB1256[B03]1:4(N=280)	5 (2.8 to 8.2)			

1 month after Vac3:PMB1256[B03] 1:4(N=279)	92.5 (88.7 to 95.3)			
Before Vaccination 1:PMB1256[B03] 1:8(N=280)	4.3 (2.2 to 7.4)			
1 month after Vac3:PMB1256[B03] 1:8(N=279)	92.5 (88.7 to 95.3)			
Before Vaccination 1:PMB1256[B03] 1:16(N=280)	4.3 (2.2 to 7.4)			
1 month after Vac3:PMB1256[B03] 1:16(N=279)	92.1 (88.3 to 95)			
Before Vaccination 1:PMB1256[B03] 1:32(N=280)	3.9 (2 to 6.9)			
1 month after Vac3:PMB1256[B03] 1:32(N=279)	81.4 (76.3 to 85.8)			
Before Vaccination 1:PMB1256[B03] 1:64(N=280)	2.9 (1.2 to 5.6)			
1 month after Vac3:PMB1256[B03] 1:64(N=279)	60.6 (54.6 to 66.3)			
Before Vaccination 1:PMB1256[B03] 1:128(N=280)	0.4 (0 to 2)			
1 month after Vac3:PMB1256[B03] 1:128(N=279)	29.4 (24.1 to 35.1)			
Before Vaccination 1:PMB866[B09] 1:4(N=277)	15.5 (11.5 to 20.3)			
1 month after Vac3:PMB866[B09] 1:4(N=276)	86.6 (82 to 90.4)			
Before Vaccination 1:PMB866[B09] 1:8(N=277)	15.2 (11.2 to 19.9)			
1 month after Vac3:PMB866[B09] 1:8(N=276)	86.2 (81.6 to 90.1)			
Before Vaccination 1:PMB866[B09] 1:16(N=277)	13.7 (9.9 to 18.3)			
1 month after Vac3:PMB866[B09] 1:16(N=276)	83.7 (78.8 to 87.9)			
Before Vaccination 1:PMB866[B09] 1:32(N=277)	8.7 (5.6 to 12.6)			
1 month after Vac3:PMB866[B09] 1:32(N=276)	54 (47.9 to 60)			
Before Vaccination 1:PMB866[B09] 1:64(N=277)	0.4 (0 to 2)			
1 month after Vac3:PMB866[B09] 1:64(N=276)	21.4 (16.7 to 26.7)			
Before Vaccination 1:PMB866[B09] 1:128(N=277)	0 (0 to 1.3)			
1 month after Vac3:PMB866[B09] 1:128(N=276)	4.3 (2.3 to 7.5)			
Before Vaccination 1:PMB431[B15] 1:4(N=275)	30.5 (25.2 to 36.4)			
1 month after Vac3:PMB431[B15] 1:4(N=281)	98.2 (95.9 to 99.4)			
Before Vaccination 1:PMB431[B15] 1:8(N=275)	28.7 (23.5 to 34.5)			
1 month after Vac3:PMB431[B15] 1:8(N=281)	98.2 (95.9 to 99.4)			
Before Vaccination 1:PMB431[B15] 1:16(N=275)	27.6 (22.4 to 33.3)			
1 month after Vac3:PMB431[B15] 1:16(N=281)	97.5 (94.9 to 99)			
Before Vaccination 1:PMB431[B15] 1:32(N=275)	21.8 (17.1 to 27.2)			
1 month after Vac3:PMB431[B15] 1:32(N=281)	85.1 (80.3 to 89)			

Before Vaccination 1:PMB431[B15] 1:64(N=275)	8.4 (5.4 to 12.3)			
1 month after Vac3:PMB431[B15] 1:64(N=281)	56.2 (50.2 to 62.1)			
Before Vaccination 1:PMB431[B15] 1:128(N=275)	0.4 (0 to 2)			
1 month after Vac3:PMB431[B15] 1:128(N=281)	19.2 (14.8 to 24.3)			
Before Vaccination 1:PMB648[B16] 1:4(N=276)	8.7 (5.7 to 12.7)			
1 month after Vac3:PMB648[B16] 1:4(N=278)	82.7 (77.8 to 87)			
Before Vaccination 1:PMB648[B16] 1:8(N=276)	7.6 (4.8 to 11.4)			
1 month after Vac3:PMB648[B16] 1:8(N=278)	81.7 (76.6 to 86)			
Before Vaccination 1:PMB648[B16] 1:16(N=276)	7.6 (4.8 to 11.4)			
1 month after Vac3:PMB648[B16] 1:16(N=278)	79.9 (74.7 to 84.4)			
Before Vaccination 1:PMB648[B16] 1:32(N=276)	6.2 (3.6 to 9.7)			
1 month after Vac3:PMB648[B16] 1:32(N=278)	54 (47.9 to 59.9)			
Before Vaccination 1:PMB648[B16] 1:64(N=276)	1.8 (0.6 to 4.2)			
1 month after Vac3:PMB648[B16] 1:64(N=278)	24.1 (19.2 to 29.6)			
Before Vaccination 1:PMB648[B16] 1:128(N=276)	0.4 (0 to 2)			
1 month after Vac3:PMB648[B16] 1:128(N=278)	5.8 (3.3 to 9.2)			

Notes:

[55] - Number of subjects analyzed signifies subjects with valid, determinate hSBA titers for given strain

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers (GMTs) for Each of the 10 Secondary Strains Before First Vaccination and 1 Month After the Third Bivalent rLP2086 Vaccination

End point title	hSBA Geometric Mean Titers (GMTs) for Each of the 10 Secondary Strains Before First Vaccination and 1 Month After the Third Bivalent rLP2086 Vaccination[56]

End point description:

Evaluable immunogenicity population. Here, N signifies subjects with valid and determinate assay results for the given antigen or strain.

End point type	Secondary

End point timeframe:

Before first vaccination, 1 month after third vaccination

Notes:

[56] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1			
Subject group type	Reporting group			
Number of subjects analysed	300[57]			
Units: titer				
geometric mean (confidence interval 95%)				
PMB3175[A29]:Before Vaccination1(N= 269)	5.7 (5.16 to 6.28)			
PMB3175[A29]:1 Month after Vaccination3(N= 278)	93.5 (84.79 to 103.09)			
PMB3010[A06]:Before Vaccination1(N= 277)	9.3 (8.68 to 9.91)			
PMB3010[A06]:1 Month after Vaccination3(N= 280)	78.6 (70.94 to 87.08)			
PMB3040[A07]:Before Vaccination1(N= 269)	11.4 (9.75 to 13.23)			
PMB3040[A07]:1 Month after Vaccination3(N= 280)	63.5 (57.93 to 69.66)			
PMB824[A12]: Before Vaccination1(N= 280)	8.4 (8.14 to 8.59)			
PMB824[A12]:1 Month after Vaccination3(N= 277)	22.3 (20.37 to 24.45)			
PMB1672[A15]:Before Vaccination1(N= 270)	5.9 (5.32 to 6.46)			
PMB1672[A15]:1 Month after Vaccination3(N= 266)	31 (27.43 to 35.07)			
PMB1989[A19]:Before Vaccination1(N= 274)	9.1 (8.7 to 9.62)			
PMB1989[A19]:1 Month after Vaccination3(N= 275)	57.6 (51.3 to 64.6)			
PMB1256[B03]:Before Vaccination1(N= 280)	4.5 (4.19 to 4.75)			
PMB1256[B03]:1 Month after Vaccination3(N= 279)	51.7 (45.36 to 58.89)			
PMB866[B09]:Before Vaccination1(N= 277)	5.2 (4.82 to 5.62)			
PMB866[B09]:1 Month after Vaccination3(N= 276)	22.9 (20.48 to 25.63)			
PMB431[B15]:Before Vaccination1(N= 275)	7.3 (6.49 to 8.23)			
PMB431[B15]:1 Month after Vaccination3(N= 281)	47.7 (43.66 to 52.16)			
PMB648[B16]:Before Vaccination1(N= 276)	4.7 (4.39 to 5.05)			
PMB648[B16]:1 Month after Vaccination3(N= 278)	22.1 (19.6 to 24.98)			

Notes:

[57] - Number of subjects analyzed signifies subjects with valid, determinate hSBA titers for given strain

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Composite hSBA Titer >=Lower Limit of Quantitation for all 4 Primary Strains Before First Vaccination and 1 Month After Second Bivalent rLP2086 Vaccination

End point title	Percentage of Subjects Achieving Composite hSBA Titer >=Lower Limit of Quantitation for all 4 Primary Strains Before

	First Vaccination and 1 Month After Second Bivalent rLP2086 Vaccination [58]

End point description:

Evaluable immunogenicity population. Here, N signifies subjects valid and determinate hSBA results on all 4 strains at the given time point.

End point type	Secondary

End point timeframe:

Before vaccination 1, 1 Month after Vaccination 2

Notes:

[58] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1			
Subject group type	Reporting group			
Number of subjects analysed	1279			
Units: percentage of subjects				
number (confidence interval 95%)				
Before First Vaccination(N= 1088)	1.1 (0.6 to 1.9)			
1 Month after Vaccination2(N= 1122)	54.1 (51.1 to 57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving at Least a 4-Fold Increase in hSBA Titer for Each of the 4 Primary Strains Before First Vaccination to 1 Month After the Second Bivalent rLP2086 Vaccination

End point title	Percentage of Subjects Achieving at Least a 4-Fold Increase in hSBA Titer for Each of the 4 Primary Strains Before First Vaccination to 1 Month After the Second Bivalent rLP2086 Vaccination [59]

End point description:

Evaluable immunogenicity population. Here, N signifies subjects with valid and determinate hSBA titers for the given strain at both the specified time point.

End point type	Secondary

End point timeframe:

One month after second Bivalent rLP2086 vaccination

Notes:

[59] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1			
Subject group type	Reporting group			
Number of subjects analysed	1279			
Units: percentage of subjects				
number (confidence interval 95%)				

PMB80[A22] (N=1223)	73.8 (71.2 to 76.2)			
PMB2001[A56] (N=1122)	84.8 (82.5 to 86.8)			
PMB2948[B24] (N=1201)	56.2 (53.3 to 59)			
PMB2707[B44] (N=1197)	55.9 (53 to 58.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving at Least a 4-Fold Increase in hSBA Titer for 2 Primary Strains Before First Vaccination to 1 Month After the Second and Third Bivalent rLP2086 Vaccination

End point title	Percentage of Subjects Achieving at Least a 4-Fold Increase in hSBA Titer for 2 Primary Strains Before First Vaccination to 1 Month After the Second and Third Bivalent rLP2086 Vaccination [60]

End point description:

Evaluable immunogenicity population. Here, N signifies subjects with valid and determinate hSBA titers for the given strain at both the specified time point.

End point type	Secondary

End point timeframe:

One month after second, third vaccination

Notes:

[60] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 2 rLP2086 Lot 2	Group 3 rLP2086 Lot 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	519	493		
Units: percentage of subjects				
number (confidence interval 95%)				
PMB80[A22]:1 Month after Vaccination2(N=493, 473)	71.2 (67 to 75.2)	74.6 (70.5 to 78.5)		
PMB80[A22]:1 Month after Vaccination3(N=501, 478)	83.8 (80.3 to 86.9)	86 (82.5 to 89)		
PMB2948[B24]:1 Month after Vaccination2(N=490,463)	56.7 (52.2 to 61.2)	56.8 (52.2 to 61.4)		
PMB2948[B24]:1 Month after Vaccination3(N=507,472)	76.5 (72.6 to 80.2)	78.4 (74.4 to 82)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers (GMTs) for 4 Primary Test Strains and for 2

Primary Test Strains and Before First Vaccination and 1 Month After the Second Bivalent rLP2086 Vaccination

End point title	hSBA Geometric Mean Titers (GMTs) for 4 Primary Test Strains and for 2 Primary Test Strains and Before First Vaccination and 1 Month After the Second Bivalent rLP2086 Vaccination [61]

End point description:

Evaluable immunogenicity population. Here N signifies subjects with valid and determinate hSBA titers for the given strain at the specified timepoint. Here, 99999 signifies geometric mean and -99999 and 99999 CI upper and lower limits for primary strains PMB2001 [A56] and PMB2707 [B44] for the reporting groups 2 and 3 as data was not planned to be analyzed for the former strains.

End point type	Secondary

End point timeframe:

Before vaccination (Vac)1, 1 Month after Vac 2

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1	Group 2 rLP2086 Lot 2	Group 3 rLP2086 Lot 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1279	519	493	
Units: titer				
geometric mean (confidence interval 95%)				
PMB80[A22]:Before Vac 1(N=1238,502,479)	12.6 (12.08 to 13.14)	12.9 (12.06 to 13.79)	12.2 (11.43 to 13.04)	
PMB80[A22]:1 Month after Vac 2(N=1263,510,487)	50.4 (47.76 to 53.09)	47.7 (43.82 to 51.97)	49.6 (45.58 to 53.99)	
PMB2001[A56]:Before Vac1(N=1135,0,0)	8.4 (7.8 to 9.05)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
PMB2001[A56]:1 Month after Vac2(N=1222,0,0)	131.2 (124.03 to 138.7)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
PMB2948[B24]:Before Vac1(N=1264,510,486)	4.5 (4.37 to 4.6)	4.6 (4.43 to 4.85)	4.6 (4.43 to 4.88)	
PMB2948[B24]:1 Month after Vac2(N=1216, 499,470)	14.3 (13.45 to 15.31)	14.5 (13.23 to 15.98)	15.2 (13.75 to 16.85)	
PMB2707[B44]:Before Vac1(N=1230,0,0)	4.3 (4.17 to 4.34)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
PMB2707[B44]:1 Month after Vac2(N=1204,0,0)	17.1 (15.8 to 18.6)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titers >=1:4,>=1:8,>=1:16,>=1:32,>=1:64,>=1:128 for Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination

End point title	Percentage of Subjects With hSBA Titers >=1:4,>=1:8,>=1:16,>=1:32,>=1:64,>=1:128 for Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination [62]

End point description:

Results for PMB80[A22] 1:16, PMB2001[A56] 1:8, PMB2948[B24] 1:8 and PMB2707[B44] 1:8 are

reported under secondary endpoint 'Percentage of Subjects With hSBA Titers >=LLOQ for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination. Evaluable immunogenicity population. Here N signifies subjects with valid and determinate hSBA titers for the given strain at the specified time point. Here, 99999 signifies number and -99999 and 99999 CI upper and lower limits for primary strains PMB2001 [A56] and PMB2707 [B44] for the reporting groups 2 and 3 as data was not planned to be analysed for the former strains.

End point type	Secondary

End point timeframe:

Before Vaccination (Vac) 1, 1 Month after Vac 2, 3

Notes:

[62] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1	Group 2 rLP2086 Lot 2	Group 3 rLP2086 Lot 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1279	519	493	
Units: percentage of subjects				
number (confidence interval 95%)				
Before Vac1:PMB80[A22]1:4(N=1238,502,479)	36.2 (33.5 to 38.9)	39.6 (35.3 to 44.1)	36.7 (32.4 to 41.2)	
1monthafterVac2:PMB80[A22]1:4(N=1263,510,487)	94.9 (93.6 to 96.1)	93.7 (91.3 to 95.7)	95.5 (93.2 to 97.1)	
1monthafterVac3:PMB80[A22]1:4(N=1266,518,492)	97.9 (97 to 98.7)	98.1 (96.5 to 99.1)	98.4 (96.8 to 99.3)	
Before Vac1:PMB80[A22]1:8(N=1238,502,479)	34.8 (32.2 to 37.5)	39 (34.8 to 43.5)	34.7 (30.4 to 39.1)	
1monthafterVac2:PMB80[A22]1:8(N=1263,510,487)	94.7 (93.3 to 95.9)	93.5 (91 to 95.5)	95.5 (93.2 to 97.1)	
1monthafterVac3:PMB80[A22]1:8(N=1266,518,492)	97.9 (97 to 98.7)	98.1 (96.5 to 99.1)	98.4 (96.8 to 99.3)	
Before Vac1:PMB80[A22]1:32(N=1238,502,47	20.9 (18.7 to 23.3)	21.7 (18.2 to 25.6)	19.8 (16.4 to 23.7)	
1monthafterVac2:PMB80[A22]1:32(N=1263,510,487)	81.9 (79.7 to 84)	79.4 (75.6 to 82.8)	80.7 (76.9 to 84.1)	
1monthafterVac3:PMB80[A22]1:32(N=1266,518,492)	93 (91.4 to 94.3)	92.1 (89.4 to 94.3)	93.1 (90.5 to 95.2)	
Before Vac1:PMB80[A22]1:64(N=1238,502,47	8.5 (7 to 10.2)	9.6 (7.1 to 12.5)	5.4 (3.6 to 7.9)	
1monthafterVac2:PMB80[A22]1:64(N=1263,510,487)	51.8 (49 to 54.6)	49.6 (45.2 to 54)	51.5 (47 to 56.1)	
1monthafterVac3:PMB80[A22]1:64(N=1266,518,492)	75.3 (72.8 to 77.6)	75.5 (71.5 to 79.1)	73.6 (69.4 to 77.4)	
Before Vac1:PMB80[A22]1:128(N=1238,502,4	2 (1.3 to 3)	2 (1 to 3.6)	2.5 (1.3 to 4.3)	
1monthafterVac2:PMB80[A22]1:128(N=1263,510,487)	24.5 (22.1 to 26.9)	23.5 (19.9 to 27.5)	24.4 (20.7 to 28.5)	
1monthafterVac3:PMB80[A22]1:128(N=1266,518,492)	48.3 (45.6 to 51.1)	46.3 (42 to 50.7)	49.2 (44.7 to 53.7)	
Before Vac1:PMB2001[A56]1:4(N=1135,0,0)	29.5 (26.9 to 32.3)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1monthafterVac2:PMB2001[A56]1:4(N=1222,0,0)	99.1 (98.4 to 99.5)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1monthafterVac3:PMB2001[A56]1:4(N=1229,0,0)	99.5 (98.9 to 99.8)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
Before Vac 1: PMB2001[A56]1:16(N=1135,0,0)	27.4 (24.8 to 30.1)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1monthafterVac2:PMB2001[A56]1:16(N=1222,0,0)	99.1 (98.4 to 99.5)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	

1monthafterVac3:PMB2001[A56]1:16(N=1229,0,0)	99.4 (98.8 to 99.8)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
Before Vac1:PMB2001[A56]1:32(N=1135,0,0)	25.6 (23 to 28.2)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac2: PMB2001[A56]1:32(N=1222,0,0)	97.2 (96.1 to 98.1)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month afterVac3:PMB2001[A56]1:32(N=1229,	98.6 (97.8 to 99.2)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
Before Vac 1:PMB2001[A56]1:64(N=1135,0,0)	17.1 (14.9 to 19.4)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month afterVac2: PMB2001[A56]1:64(N=1222,0,0)	89.4 (87.6 to 91.1)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac3: PMB2001[A56]1:64(N=1229,0,0)	94.5 (93 to 95.7)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
Before Vac 1:PMB2001[A56]1:128(N=1135,0,0)	6.4 (5.1 to 8)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac2:PMB2001[A56]1:128(N=1222,0,0)	63.4 (60.6 to 66.1)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month afterVac3:PMB2001[A56]1:128(N=1229	82.9 (80.7 to 85)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
Before Vac1:PMB2948[B24]1:4(N=1264,510,4	6.8 (5.5 to 8.3)	10.2 (7.7 to 13.2)	9.5 (7 to 12.4)	
1monthafterVac2:PMB2948[B24]1:4(N=1216,499,470)	69.2 (66.6 to 71.8)	72.9 (68.8 to 76.8)	74 (69.8 to 78)	
1monthafterVac3:PMB2948[B24]1:4(N=1250,516,479)	88.9 (87 to 90.6)	89.9 (87 to 92.4)	91.6 (88.8 to 94)	
Before Vac1:PMB2948[B24]1:16(N=1264,510,	5.4 (4.2 to 6.8)	7.5 (5.3 to 10.1)	7 (4.9 to 9.6)	
1monthafterVac2:PMB2948[B24]1:16(N=1216,499,470)	60 (57.2 to 62.8)	61.5 (57.1 to 65.8)	62.1 (57.6 to 66.5)	
1monthafterVac3:PMB2948[B24]1:16(N=1250,516,479)	82.6 (80.4 to 84.7)	81.2 (77.6 to 84.5)	83.1 (79.4 to 86.3)	
Before Vac1:PMB2948[B24]1:32(N=1264,510,	2.8 (2 to 3.9)	3.9 (2.4 to 6)	3.7 (2.2 to 5.8)	
1monthafterVac2:PMB2948[B24]1:32(N=1216,499,470)	33 (30.3 to 35.7)	34.5 (30.3 to 38.8)	35.5 (31.2 to 40)	
1monthafterVac3:PMB2948[B24]1:32(N=1250,516,479)	52.1 (49.3 to 54.9)	54.8 (50.4 to 59.2)	54.1 (49.5 to 58.6)	
Before Vac1:PMB2948[B24]1:64(N=1264,510,	1.3 (0.7 to 2)	1.2 (0.4 to 2.5)	1.9 (0.9 to 3.5)	
1monthafterVac2:PMB2948[B24]1:64(N=1216,499,470)	15.3 (13.3 to 17.4)	13 (10.2 to 16.3)	15.3 (12.2 to 18.9)	
1monthafterVac3:PMB2948[B24]1:64(N=1250,516,479)	22.8 (20.5 to 25.2)	27.5 (23.7 to 31.6)	25.3 (21.4 to 29.4)	
Before Vac1:PMB2948[B24]1:128(N=1264,510	0.5 (0.2 to 1)	0.2 (0 to 1.1)	0.4 (0 to 1.5)	
1monthafterVac2:PMB2948[B24]1:128(N=1216,499,470)	6.2 (4.9 to 7.7)	5.2 (3.4 to 7.5)	7 (4.9 to 9.7)	
1monthafterVac3:PMB2948[B24]1:128(N=1250,516,479)	8.9 (7.4 to 10.6)	11.2 (8.6 to 14.3)	8.6 (6.2 to 11.4)	
Before Vac1:PMB2707[B44]1:4(N=1230,0,0)	4.6 (3.5 to 5.9)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1month after Vac2:PMB2707[B44]1:4(N=1204,0,0)	66.7 (64 to 69.4)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1month after Vac3:PMB2707[B44]1:4(N=1210.0,0)	90.4 (88.6 to 92)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
Before Vac1:PMB2707[B44]1:16(N=1230,0,0)	3 (2.1 to 4.1)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac2: PMB2707[B44]1:16(N=1204,0,0)	57.7 (54.9 to 60.5)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac3:PMB2707[B44]1:16(N=1210,0,0)	86.8 (84.7 to 88.6)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	

Before Vac 1:PMB2707[B44]1:32(N=1230,0,0)	1.6 (1 to 2.5)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac2:PMB2707[B44]1:32(N=1204,0,0)	39 (36.3 to 41.9)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac3: PMB2707[B44]1:32(N=1210,0,0)	71.6 (68.9 to 74.1)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
Before Vac 1:PMB2707[B44]1:64(N=1230,0,0)	0.7 (0.3 to 1.3)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac2:PMB2707[B44]1:64(N=1204,0,0)	23.3 (21 to 25.8)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac3:PMB2707[B44]1:64(N=1210,0,0)	54.5 (51.7 to 57.4)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
Before Vac 1:PMB2707[B44]1:128(N=1230,0,0)	0.2 (0 to 0.6)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac2:PMB2707[B44]1:128(N=1204,0,0)	13 (11.2 to 15.1)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac3:PMB2707[B44]1:128(N=1210,0,0)	35 (32.4 to 37.8)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving at Least a 3-Fold Increase in hSBA Titer for 4 Primary Test Strains and for Primary Test Starins Before First Vaccination to 1 Month After Third Bivalent rLP2086 Vaccination

End point title	Percentage of Subjects Achieving at Least a 3-Fold Increase in hSBA Titer for 4 Primary Test Strains and for Primary Test Starins Before First Vaccination to 1 Month After Third Bivalent rLP2086 Vaccination[63]

End point description:

Data was not reported because 3-fold rise analyses was not performed as per change in planned analysis.

End point type	Secondary

End point timeframe:

One month after third bivalent rLP2086 vaccination

Notes:

[63] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1	Group 2 rLP2086 Lot 2	Group 3 rLP2086 Lot 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[64]	0[65]	0[66]	
Units: percentage of subjects				
number (confidence interval 95%)				

Notes:

[64] - 3-Fold rise analyses was not performed as per change in planned analysis.

[65] - 3-Fold rise analyses was not performed as per change in planned analysis.

[66] - 3-Fold rise analyses was not performed as per change in planned analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving at Least a 2-Fold Increase in hSBA Titer for 4 Primary Test Strains and for 2 Primary Test Starins Before First Vaccination to 1 Month After the Third Bivalent rLP2086 Vaccination

End point title	Percentage of Subjects Achieving at Least a 2-Fold Increase in hSBA Titer for 4 Primary Test Strains and for 2 Primary Test Starins Before First Vaccination to 1 Month After the Third Bivalent rLP2086 Vaccination [67]

End point description:

Evaluable immunogenicity population. Here N signifies subjects with valid and determinate hSBA titers for the given strain at the specified timepoint. Here, 99999 signifies number and -99999 and 99999 CI upper and lower limits for primary strains PMB2001 [A56] and PMB2707 [B44] for the reporting groups 2 and 3 as data was not planned to be analysed for the former strains.

End point type	Secondary

End point timeframe:

One month after third bivalent rLP2086 vaccination (Vac)

Notes:

[67] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1	Group 2 rLP2086 Lot 2	Group 3 rLP2086 Lot 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1279	519	493	
Units: percentage of subjects				
number (confidence interval 95%)				
PMB80[A22]:1 Month after Vac 3(N=1225,501,478)	91.43 (89.7 to 92.9)	92.02 (89.3 to 94.2)	93.51 (90.9 to 95.6)	
PMB2001[A56]:1 Month after Vac 3(N=1128,0,0)	95.04 (93.6 to 96.2)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
PMB2948[B24]:1 Month after Vac 3(N=1235,507,472)	81.05 (78.8 to 83.2)	79.09 (75.3 to 82.6)	80.93 (77.1 to 84.4)	
PMB2707[B44]:1 Month after Vac 3(N=1203,0,0)	86.62 (84.6 to 88.5)	99999 (-99999 to 99999)	-99999 (-99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With hSBA Titers >=LLOQ for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination

End point title	Percentage of Subjects With hSBA Titers >=LLOQ for 4 Primary Test Strains Before First Vaccination, 1 Month After Second and Third Bivalent rLP2086 Vaccination[68]

End point description:

Evaluable immunogenicity population. Here N signifies subjects with valid and determinate hSBA titers for the given strain at the specified time point. Here, 99999 signifies number and -99999 and 99999 CI upper and lower limits for primary strains PMB2001 [A56] and PMB2707 [B44] for the reporting groups 2 and 3 as data was not planned to be analysed for the former strains.

End point type	Secondary

End point timeframe:

Before Vaccination (Vac) 1, 1 Month after Vac 2, 3

Notes:

[68] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Group 1 rLP2086 Lot 1	Group 2 rLP2086 Lot 2	Group 3 rLP2086 Lot 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1279	519	493	
Units: percentage of subjects				
number (confidence interval 95%)				
Before Vac 1: PMB80[A22] 1:16(N=1238, 502, 479)	33.2 (30.6 to 35.9)	34.9 (30.7 to 39.2)	31.7 (27.6 to 36.1)	
1month after Vac2:PMB80[A22] 1:16(N=1263,510,487)	94.3 (92.9 to 95.5)	92.7 (90.1 to 94.8)	94.7 (92.3 to 96.5)	
1month after Vac3:PMB80[A22]1:16(N=1266,518,49	97.8 (96.8 to 98.5)	97.3 (95.5 to 98.5)	98.2 (96.6 to 99.2)	
Before Vac 1: PMB2001[A56] 1:8(N=1135,0,0)	27.5 (24.9 to 30.2)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac2:PMB2001[A56]1:8(N=1222,0,0)	99.1 (98.4 to 99.5)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1 month after Vac3:PMB2001[A56]1:8(N=1229,0,0)	99.5 (98.9 to 99.8)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
Before Vac 1: PMB2948[B24]1:8(N=1264,510,486)	6.4 (5.1 to 7.9)	8.6 (6.3 to 11.4)	8.4 (6.1 to 11.3)	
1month after Vac2:PMB2948[B24]1:8(N=1216,499,4	66.4 (63.6 to 69)	70.1 (65.9 to 74.1)	70.2 (65.9 to 74.3)	
1month after Vac3:PMB2948[B24]1:8(N=1250,516,4	87.1 (85.1 to 88.9)	87.6 (84.4 to 90.3)	90 (86.9 to 92.5)	
Before Vac 1: PMB2707[B44]1:8(N=1230,0,0)	3.6 (2.6 to 4.8)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1month after Vac2: PMB2707[B44]1:8(N=1204,0,0)	64 (61.3 to 66.8)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	
1month after Vac3: PMB2707[B44]1:8(N=1210,0,0)	89.3 (87.4 to 90.9)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs/SAEs: recorded from first vaccination through 6 months after third vaccination. Subjects recorded pre-specified reactogenicity events (local reactions, systemic events) in electronic diary within 7 days after first, second and third vaccination

Adverse event reporting additional description:

All AEs collected on case report form are shown below as having been collected via non-systematic assessment. All events reported via electronic diary (reactogenicity events) are shown below as having been collected via systematic assessment. Reactogenicity events are grouped by all severities and doses combined.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Group 1 rLP2086 Lot 1

Reporting group description:

Lot 1 on a 0-, 2-, 6- month schedule.

Reporting group title	Group 3 rLP2086 Lot 3

Reporting group description:

Lot 3 on a 0-, 2-, 6- month schedule.

Reporting group title	Group 4 HAV/Saline

Reporting group description:

Hepatitis A virus vaccine (HAV) on a 0- and 6-month schedule and saline at Month 2.

Reporting group title	Group 2 rLP2086 Lot 2

Reporting group description:

Lot 2 on a 0-, 2-, 6- month schedule

Serious adverse events	Group 1 rLP2086 Lot 1	Group 3 rLP2086 Lot 3	Group 4 HAV/Saline
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 1508 (1.46%)	19 / 587 (3.24%)	22 / 897 (2.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Pregnancy, puerperium and perinatal conditions			
Abortion threatened			

subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	0 / 897 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Testicular torsion			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	0 / 897 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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			
Suicidal ideation			
subjects affected / exposed	1 / 1508 (0.07%)	1 / 587 (0.17%)	2 / 897 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorexia nervosa			

subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Depression suicidal			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Mental disorder			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Aggression			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	0 / 897 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety disorder			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Borderline personality disorder			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			

subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Heart sounds abnormal			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Injury, poisoning and procedural complications			
Forearm fracture			
subjects affected / exposed	2 / 1508 (0.13%)	1 / 587 (0.17%)	0 / 897 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol poisoning			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Bone contusion			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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

Humerus fracture			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Laceration			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck injury			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Skull fracture			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Tibia fracture			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Wrist fracture			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Cardiac disorders			

Ventricular extrasystoles			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Nervous system disorders			
Complex partial seizures			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Headache			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	0 / 897 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple sclerosis			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Syncope			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Eye disorders			
Blindness transient			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 1508 (0.13%)	1 / 587 (0.17%)	0 / 897 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			

subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Pancreatitis			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	0 / 897 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Musculoskeletal and connective tissue disorders			
Synovial cyst			

subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	4 / 897 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	1 / 1508 (0.07%)	1 / 587 (0.17%)	0 / 897 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	2 / 897 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Abscess limb			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess neck			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	0 / 897 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendiceal abscess			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Bronchitis			

subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Influenza			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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
Meningitis aseptic			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Osteomyelitis			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 1508 (0.07%)	0 / 587 (0.00%)	0 / 897 (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
Viral infection			

subjects affected / exposed	0 / 1508 (0.00%)	0 / 587 (0.00%)	1 / 897 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 1508 (0.00%)	1 / 587 (0.17%)	0 / 897 (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

Serious adverse events	Group 2 rLP2086 Lot 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 598 (1.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion threatened			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 598 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Testicular torsion			
subjects affected / exposed	1 / 598 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anorexia nervosa			
subjects affected / exposed	1 / 598 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Depression suicidal			
subjects affected / exposed	1 / 598 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mental disorder			
subjects affected / exposed	1 / 598 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aggression			

subjects affected / exposed	1 / 598 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anxiety disorder			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Borderline personality disorder			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychotic disorder			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Major depression			
subjects affected / exposed	1 / 598 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Heart sounds abnormal			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Forearm fracture			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Alcohol poisoning				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone contusion				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laceration				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neck injury				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post-traumatic neck syndrome				

subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skull fracture				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Ventricular extrasystoles				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Complex partial seizures				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 598 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple sclerosis				

subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Blindness transient				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenitis				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				

Cholecystitis			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 598 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Synovial cyst			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis perforated			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abscess			

subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess limb				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess neck				
subjects affected / exposed	1 / 598 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Appendiceal abscess				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis aseptic				
subjects affected / exposed	0 / 598 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				

subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 598 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1 rLP2086 Lot 1	Group 3 rLP2086 Lot 3	Group 4 HAV/Saline
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1410 / 1508 (93.50%)	542 / 587 (92.33%)	655 / 897 (73.02%)
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed	42 / 1508 (2.79%)	9 / 587 (1.53%)	20 / 897 (2.23%)
occurrences (all)	45	10	22
Ligament sprain			
subjects affected / exposed	36 / 1508 (2.39%)	8 / 587 (1.36%)	24 / 897 (2.68%)
occurrences (all)	42	8	25
Contusion			
subjects affected / exposed	20 / 1508 (1.33%)	6 / 587 (1.02%)	19 / 897 (2.12%)
occurrences (all)	20	6	19
Muscle strain			
subjects affected / exposed	7 / 1508 (0.46%)	1 / 587 (0.17%)	9 / 897 (1.00%)
occurrences (all)	8	1	10
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 1508 (0.33%)	3 / 587 (0.51%)	3 / 897 (0.33%)
occurrences (all)	5	3	3
Headache			
subjects affected / exposed	42 / 1508 (2.79%)	15 / 587 (2.56%)	23 / 897 (2.56%)
occurrences (all)	46	17	29
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	18 / 1508 (1.19%)	5 / 587 (0.85%)	8 / 897 (0.89%)
occurrences (all)	19	5	9
Fatigue			
subjects affected / exposed	5 / 1508 (0.33%)	6 / 587 (1.02%)	5 / 897 (0.56%)
occurrences (all)	6	6	6
Fever >=38.0 degrees C -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[1]	154 / 1504 (10.24%)	57 / 585 (9.74%)	46 / 892 (5.16%)
occurrences (all)	154	57	46
Vomiting -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			

subjects affected / exposed[2]	110 / 1504 (7.31%)	44 / 585 (7.52%)	41 / 893 (4.59%)
occurrences (all)	110	44	41
Diarrhea-Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[3]	294 / 1504 (19.55%)	117 / 585 (20.00%)	187 / 893 (20.94%)
occurrences (all)	294	117	187
Headache -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[4]	1032 / 1504 (68.62%)	392 / 585 (67.01%)	477 / 893 (53.42%)
occurrences (all)	1032	392	477
Fatigue -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[5]	1011 / 1504 (67.22%)	369 / 585 (63.08%)	454 / 893 (50.84%)
occurrences (all)	1011	369	454
Chills-Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[6]	566 / 1504 (37.63%)	225 / 585 (38.46%)	227 / 893 (25.42%)
occurrences (all)	566	225	227
Muscle pain -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[7]	598 / 1504 (39.76%)	210 / 585 (35.90%)	254 / 893 (28.44%)
occurrences (all)	598	210	254
Joint pain -Any (reactogenicity	Additional description: Subjects affected and		

event)	occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[8]	532 / 1504 (35.37%)	191 / 585 (32.65%)	209 / 893 (23.40%)
occurrences (all)	532	191	209
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	29 / 1508 (1.92%)	9 / 587 (1.53%)	8 / 897 (0.89%)
occurrences (all)	29	10	8
Diarrhoea			
subjects affected / exposed	15 / 1508 (0.99%)	3 / 587 (0.51%)	15 / 897 (1.67%)
occurrences (all)	15	3	16
Vomiting			
subjects affected / exposed	14 / 1508 (0.93%)	2 / 587 (0.34%)	12 / 897 (1.34%)
occurrences (all)	15	2	14
Nausea			
subjects affected / exposed	10 / 1508 (0.66%)	3 / 587 (0.51%)	7 / 897 (0.78%)
occurrences (all)	11	3	7
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	19 / 1508 (1.26%)	7 / 587 (1.19%)	9 / 897 (1.00%)
occurrences (all)	19	8	9
Rhinitis allergic			
subjects affected / exposed	16 / 1508 (1.06%)	7 / 587 (1.19%)	14 / 897 (1.56%)
occurrences (all)	18	8	15
Oropharyngeal pain			
subjects affected / exposed	19 / 1508 (1.26%)	5 / 587 (0.85%)	6 / 897 (0.67%)
occurrences (all)	23	5	6
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	14 / 1508 (0.93%)	14 / 587 (2.39%)	11 / 897 (1.23%)
occurrences (all)	14	14	12
Dermatitis contact			
subjects affected / exposed	14 / 1508 (0.93%)	5 / 587 (0.85%)	5 / 897 (0.56%)
occurrences (all)	15	6	5

Pain at injection site -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for LR is same as data collected through ediaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[9]	1403 / 1504 (93.28%)	541 / 585 (92.48%)	525 / 897 (58.53%)
occurrences (all)	1403	541	525
Redness -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for LR is same as data collected through ediaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[10]	365 / 1504 (24.27%)	145 / 585 (24.79%)	21 / 893 (2.35%)
occurrences (all)	365	145	21
Swelling -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for LR is same as data collected through ediaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[11]	416 / 1504 (27.66%)	158 / 585 (27.01%)	26 / 893 (2.91%)
occurrences (all)	416	158	26
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	18 / 1508 (1.19%)	3 / 587 (0.51%)	13 / 897 (1.45%)
occurrences (all)	18	3	13
Pain in extremity			
subjects affected / exposed	13 / 1508 (0.86%)	2 / 587 (0.34%)	12 / 897 (1.34%)
occurrences (all)	13	2	12
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	105 / 1508 (6.96%)	45 / 587 (7.67%)	70 / 897 (7.80%)
occurrences (all)	122	50	81
Pharyngitis			
subjects affected / exposed	69 / 1508 (4.58%)	24 / 587 (4.09%)	43 / 897 (4.79%)
occurrences (all)	76	27	52
Nasopharyngitis			
subjects affected / exposed	59 / 1508 (3.91%)	32 / 587 (5.45%)	32 / 897 (3.57%)
occurrences (all)	70	36	36
Gastroenteritis			

subjects affected / exposed	43 / 1508 (2.85%)	19 / 587 (3.24%)	25 / 897 (2.79%)
occurrences (all)	47	21	29
Bronchitis			
subjects affected / exposed	27 / 1508 (1.79%)	10 / 587 (1.70%)	19 / 897 (2.12%)
occurrences (all)	29	10	20
Sinusitis			
subjects affected / exposed	34 / 1508 (2.25%)	14 / 587 (2.39%)	22 / 897 (2.45%)
occurrences (all)	41	16	22
Otitis media			
subjects affected / exposed	19 / 1508 (1.26%)	11 / 587 (1.87%)	16 / 897 (1.78%)
occurrences (all)	20	11	16
Pharyngitis streptococcal			
subjects affected / exposed	21 / 1508 (1.39%)	10 / 587 (1.70%)	13 / 897 (1.45%)
occurrences (all)	25	11	13
Influenza			
subjects affected / exposed	19 / 1508 (1.26%)	8 / 587 (1.36%)	9 / 897 (1.00%)
occurrences (all)	19	8	9
Acute sinusitis			
subjects affected / exposed	18 / 1508 (1.19%)	7 / 587 (1.19%)	7 / 897 (0.78%)
occurrences (all)	20	7	7
Urinary tract infection			
subjects affected / exposed	18 / 1508 (1.19%)	10 / 587 (1.70%)	7 / 897 (0.78%)
occurrences (all)	19	10	7
Viral infection			
subjects affected / exposed	15 / 1508 (0.99%)	4 / 587 (0.68%)	12 / 897 (1.34%)
occurrences (all)	16	4	14
Viral pharyngitis			
subjects affected / exposed	19 / 1508 (1.26%)	2 / 587 (0.34%)	9 / 897 (1.00%)
occurrences (all)	25	2	11
Tonsillitis			
subjects affected / exposed	10 / 1508 (0.66%)	3 / 587 (0.51%)	10 / 897 (1.11%)
occurrences (all)	11	4	10
Otitis externa			
subjects affected / exposed	8 / 1508 (0.53%)	3 / 587 (0.51%)	9 / 897 (1.00%)
occurrences (all)	8	3	9
Otitis media acute			

subjects affected / exposed	8 / 1508 (0.53%)	2 / 587 (0.34%)	10 / 897 (1.11%)
occurrences (all)	9	2	11
Gastroenteritis viral			
subjects affected / exposed	8 / 1508 (0.53%)	1 / 587 (0.17%)	9 / 897 (1.00%)
occurrences (all)	9	1	9

Non-serious adverse events	Group 2 rLP2086 Lot 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	547 / 598 (91.47%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	19 / 598 (3.18%)		
occurrences (all)	20		
Ligament sprain			
subjects affected / exposed	14 / 598 (2.34%)		
occurrences (all)	15		
Contusion			
subjects affected / exposed	7 / 598 (1.17%)		
occurrences (all)	7		
Muscle strain			
subjects affected / exposed	5 / 598 (0.84%)		
occurrences (all)	5		
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 598 (1.00%)		
occurrences (all)	6		
Headache			
subjects affected / exposed	21 / 598 (3.51%)		
occurrences (all)	23		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	8 / 598 (1.34%)		
occurrences (all)	8		
Fatigue			
subjects affected / exposed	3 / 598 (0.50%)		
occurrences (all)	3		

Fever >=38.0 degrees C -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[1]	52 / 597 (8.71%)		
occurrences (all)	52		
Vomiting -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[2]	31 / 597 (5.19%)		
occurrences (all)	31		
Diarrhea-Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[3]	114 / 597 (19.10%)		
occurrences (all)	114		
Headache -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[4]	379 / 597 (63.48%)		
occurrences (all)	379		
Fatigue -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[5]	380 / 597 (63.65%)		
occurrences (all)	380		
Chills-Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			

subjects affected / exposed[6]	183 / 597 (30.65%)		
occurrences (all)	183		
Muscle pain -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[7]	205 / 597 (34.34%)		
occurrences (all)	205		
Joint pain -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for SE is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Systemic Events 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[8]	170 / 597 (28.48%)		
occurrences (all)	170		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 598 (0.84%)		
occurrences (all)	5		
Diarrhoea			
subjects affected / exposed	6 / 598 (1.00%)		
occurrences (all)	6		
Vomiting			
subjects affected / exposed	4 / 598 (0.67%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	7 / 598 (1.17%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	9 / 598 (1.51%)		
occurrences (all)	9		
Rhinitis allergic			
subjects affected / exposed	7 / 598 (1.17%)		
occurrences (all)	7		
Oropharyngeal pain			

subjects affected / exposed	3 / 598 (0.50%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	6 / 598 (1.00%)		
occurrences (all)	6		
Dermatitis contact			
subjects affected / exposed	7 / 598 (1.17%)		
occurrences (all)	7		
Pain at injection site -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for LR is same as data collected through ediaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[9]	544 / 597 (91.12%)		
occurrences (all)	544		
Redness -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for LR is same as data collected through ediaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[10]	136 / 597 (22.78%)		
occurrences (all)	136		
Swelling -Any (reactogenicity event)	Additional description: Subjects affected and occurrences for LR is same as data collected through ediaries cannot be used to distinguish one occurrence from another within a subject/vaccination.		
alternative dictionary used: Local Reactions 0.0			
alternative assessment type: Systematic			
subjects affected / exposed[11]	161 / 597 (26.97%)		
occurrences (all)	161		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 598 (1.84%)		
occurrences (all)	12		
Pain in extremity			
subjects affected / exposed	3 / 598 (0.50%)		
occurrences (all)	3		
Infections and infestations			

Upper respiratory tract infection				
subjects affected / exposed	53 / 598 (8.86%)			
occurrences (all)	57			
Pharyngitis				
subjects affected / exposed	21 / 598 (3.51%)			
occurrences (all)	22			
Nasopharyngitis				
subjects affected / exposed	32 / 598 (5.35%)			
occurrences (all)	42			
Gastroenteritis				
subjects affected / exposed	25 / 598 (4.18%)			
occurrences (all)	29			
Bronchitis				
subjects affected / exposed	6 / 598 (1.00%)			
occurrences (all)	6			
Sinusitis				
subjects affected / exposed	19 / 598 (3.18%)			
occurrences (all)	22			
Otitis media				
subjects affected / exposed	11 / 598 (1.84%)			
occurrences (all)	13			
Pharyngitis streptococcal				
subjects affected / exposed	6 / 598 (1.00%)			
occurrences (all)	6			
Influenza				
subjects affected / exposed	9 / 598 (1.51%)			
occurrences (all)	9			
Acute sinusitis				
subjects affected / exposed	8 / 598 (1.34%)			
occurrences (all)	9			
Urinary tract infection				
subjects affected / exposed	5 / 598 (0.84%)			
occurrences (all)	5			
Viral infection				
subjects affected / exposed	8 / 598 (1.34%)			
occurrences (all)	9			

Viral pharyngitis			
subjects affected / exposed	4 / 598 (0.67%)		
occurrences (all)	5		
Tonsillitis			
subjects affected / exposed	7 / 598 (1.17%)		
occurrences (all)	11		
Otitis externa			
subjects affected / exposed	9 / 598 (1.51%)		
occurrences (all)	9		
Otitis media acute			
subjects affected / exposed	6 / 598 (1.00%)		
occurrences (all)	6		
Gastroenteritis viral			
subjects affected / exposed	3 / 598 (0.50%)		
occurrences (all)	3		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here, number of subjects exposed signifies subjects with known values after the vaccination.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here, number of subjects exposed signifies subjects with known values after the vaccination.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here, number of subjects exposed signifies subjects with known values after the vaccination.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here, number of subjects exposed signifies subjects with known values after the vaccination.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here, number of subjects exposed signifies subjects with known values after the vaccination.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here, number of subjects exposed signifies subjects with known values after the vaccination.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here, number of subjects exposed signifies subjects with known values after the vaccination.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here, number of subjects exposed signifies subjects with known values after the vaccination.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here, number of subjects exposed signifies subjects with known values after the vaccination.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here, number of subjects exposed signifies subjects with known values after the vaccination.
[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here, number of subjects exposed signifies subjects with known values after the vaccination.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 September 2012	Footnotes added to the schedule of activities regarding contacting subjects to follow-up diary events persisting after day 7 of the e-diary and regarding the checklist for AE reporting.
24 September 2012	Adverse event reporting requirements updated - Serious adverse events occurring to a subject after the active reporting period has ended should be reported to the sponsor if the investigator becomes aware of them; at a minimum, all serious adverse events that the investigator believes have at least a reasonable possibility of being related to study drug are to be reported to the sponsor.
24 September 2012	Added details on inquiries about medical visits and missed days of school and work associated with adverse events to Procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported