Clinical trial results:
A Study in Healthy, Young Adults and Healthy Infants of the Safety, Tolerability, and Immunogenicity of a Recombinant Hepatitis B Vaccine Manufactured by an Investigational Process

Summary

EudraCT number	2005-005939-10
Trial protocol	FI
Global end of trial date	10 May 2007

Results information

Result version number	v1 (current)
This version publication date	07 December 2016
First version publication date	07 December 2016

Trial information

Trial identification

Sponsor protocol code	V232-055

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	10 May 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 May 2007
Global end of trial reached?	Yes
Global end of trial date	10 May 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this trial were: Stage 1 assessed the safety and tolerability of glutathione (GSH)/2X phosphate process hepatitis B vaccine in healthy adults and Stage 2 evaluated the immunogenicity of the GSH/2X phosphate hepatitis B vaccine compared with the 2X phosphate hepatitis B vaccine in healthy infants who received the vaccine on a 0-, 1-, and 6-month schedule.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research. Stage 2 was conducted in healthy infants, conditional upon satisfactory review of all vaccine-related serious adverse experiences (SAEs) that may have occurred after the first vaccine dose in participants from Stage 1 over the 14-day safety follow-up period.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 May 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 300
Worldwide total number of subjects	300
EEA total number of subjects	300

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)	240
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	60

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 6 clinical sites in Finland. Sixty adult participants were enrolled in Stage 1 and 240 healthy infant participants, 2 to 4 months of age, were enrolled in Stage 2 of this study.

Pre-assignment

Screening details:

Stage 1: participants 20 to 35 years of age in good health based on a medical history. Stage 2: healthy infants 2 to 4 months old.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults

Arm description:

Participants received a 3 x 10-µg regimen of GSH/2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 1.0-mL intramuscular injection.

Arm type	Experimental
Investigational medicinal product name	GSH/2X Phosphate Hepatitis B Vaccine
Investigational medicinal product code	
Other name	V232
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a 3 x 10-µg regimen of GSH/2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 1.0-mL intramuscular injection

Arm title	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults

Arm description:

Participants received a 3 x 10-µg regimen of 2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 1.0-mL intramuscular injection

Arm type	Active comparator
Investigational medicinal product name	2X Phosphate Hepatitis B Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a 3 x 10-µg regimen of 2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 1.0-mL intramuscular injection

Arm title	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants

Arm description:

Participants received a 3 x 5-µg regimen of GSH/2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 0.5-mL intramuscular injection

Arm type	Experimental

Investigational medicinal product name	GSH/2X Phosphate Hepatitis B Vaccine
Investigational medicinal product code	
Other name	V232
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a 3 x 5-µg regimen of GSH/2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 0.5-mL intramuscular injection

Arm title	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants

Arm description:

Participants received a 3 x 5-µg regimen of 2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6- month schedule, as a 0.5-mL intramuscular injection.

Arm type	Active comparator
Investigational medicinal product name	2X Phosphate Hepatitis B Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received a 3 x 5-µg regimen of 2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 0.5-mL intramuscular injection.

Number of subjects in period 1	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants
Started	50	10	120
Received all 3 Vaccinations	47	9	119
Completed	47	8	118
Not completed	3	2	2
Consent withdrawn by subject	1	-	1
Adverse event, non-fatal	1	1	-
Lost to follow-up	-	1	1
Protocol deviation	1	-	-

Number of subjects in period 1	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants
Started	120
Received all 3 Vaccinations	118
Completed	118
Not completed	2
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Lost to follow-up	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults
Reporting group description:	
Participants received a 3 x 10-µg regimen of GSH/2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 1.0-mL intramuscular injection.	
Reporting group title	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults
Reporting group description:	
Participants received a 3 x 10-µg regimen of 2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 1.0-mL intramuscular injection	
Reporting group title	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants
Reporting group description:	
Participants received a 3 x 5-µg regimen of GSH/2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 0.5-mL intramuscular injection	
Reporting group title	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants
Reporting group description:	
Participants received a 3 x 5-µg regimen of 2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6- month schedule, as a 0.5-mL intramuscular injection.	

Reporting group values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants
Number of subjects	50	10	120
Age Categorical			
Units: Subjects			
2 to 4 months	0	0	120
20 to 35 years	50	10	0
Age Continuous			
Units: years			
arithmetic mean	27.1	25.5	0.3
standard deviation	± 4.3	± 2.9	± 0
Gender Categorical			
Units: Subjects			
Male	16	4	71
Female	34	6	49

Reporting group values	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants	Total	
Number of subjects	120	300	
Age Categorical			
Units: Subjects			
2 to 4 months	120	240	
20 to 35 years	0	60	
Age Continuous			
Units: years			
arithmetic mean	0.2		
standard deviation	± 0.1	-	
Gender Categorical			
Units: Subjects			
Male	56	147	

Female	64	153	

End points

End points reporting groups

Reporting group title	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults
Reporting group description:	
Participants received a 3 x 10-µg regimen of GSH/2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 1.0-mL intramuscular injection.	
Reporting group title	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults
Reporting group description:	
Participants received a 3 x 10-µg regimen of 2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 1.0-mL intramuscular injection	
Reporting group title	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants
Reporting group description:	
Participants received a 3 x 5-µg regimen of GSH/2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 0.5-mL intramuscular injection	
Reporting group title	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants
Reporting group description:	
Participants received a 3 x 5-µg regimen of 2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6- month schedule, as a 0.5-mL intramuscular injection.	

Primary: Percentage of Participants Who Experienced One or More Adverse Events (AEs, Stage 1 Adults)

End point title	Percentage of Participants Who Experienced One or More Adverse Events (AEs, Stage 1 Adults)[1][2]
End point description:	
An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. The safety population consisted of all adult participants who received at least one dose of GSH/2X Phosphate Hepatitis B Vaccine or 2X Phosphate Hepatitis B Vaccine.	
End point type	Primary
End point timeframe:	
Up to 7 months	

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: No statistical analysis was planned or performed for this end point.

[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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	10		
Units: Percentage of Participants				
number (not applicable)	94	90		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Discontinuing Study Drug Due to AEs (Stage 1 Adults)

End point title	Percentage of Participants Discontinuing Study Drug Due to AEs (Stage 1 Adults)[3][4]

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. The safety population consisted of all adult participants who received at least one dose of GSH/2X Phosphate Hepatitis B Vaccine or 2X Phosphate Hepatitis B Vaccine.

End point type	Primary

End point timeframe:

Up to Month 6

Notes:

[3] - 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: No statistical analysis was planned or performed for this end point.

[4] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	10		
Units: Percentage of Participants				
number (not applicable)	2	0		

Statistical analyses

No statistical analyses for this end point

Primary: Seroprotection rate (SPR, Percentage of Participants with Anti-HBs Titer ≥10 mIU/mL) (Stage 2 Infants)

End point title	Seroprotection rate (SPR, Percentage of Participants with Anti-HBs Titer ≥10 mIU/mL) (Stage 2 Infants)[5][6]

End point description:

SPR is defined as the percentage of participants who demonstrate antibodies to hepatitis B surface antigen ≥10 mIU/mL. A Hepatitis B enhanced chemiluminescence assay was used in this antibody analysis. The statistical criterion for an adequate SPR required the lower bound of the 2-sided multiplicity adjusted 95.0% confidence interval have a lower bound that exceeds 90.0%. Per protocol population was defined as the infant participants who met the inclusion criteria, were not protocol violators, were seronegative at baseline (prevaccination anti-HBs titer <5 mIU/mL), and had serology and vaccinations within the specified day ranges.

End point type	Primary

End point timeframe:

Month 7 (1 month post-dose 3)

Notes:

[5] - 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: No statistical analysis was planned or performed for this end point.

[6] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	112		
Units: Percentage of Participants				
number (confidence interval 95%)	100 (99.5 to 100)	100 (99.6 to 100)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Any Quantifiable Anti-HBs (anti-HBs titers ≥ 5 mIU/mL) (Stage 2 Infants)

End point title	Percentage of Participants with Any Quantifiable Anti-HBs (anti-HBs titers ≥ 5 mIU/mL) (Stage 2 Infants)[7][8]

End point description:

A Hepatitis B enhanced chemiluminescence assay was used in this antibody analysis. Per protocol population was defined as the infant participants who met the inclusion criteria, were not protocol violators, were seronegative at baseline (prevaccination anti-HBs titer <5 mIU/mL), and had serology and vaccinations within the specified day ranges

End point type	Primary

End point timeframe:

Month 7 (1 month post-dose 3)

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: No statistical analysis was planned or performed for this end point.

[8] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	112		
Units: Percentage of Participants				
number (confidence interval 95%)	100 (99.5 to 100)	100 (99.6 to 100)		

Statistical analyses

No statistical analyses for this end point

Primary: Anti-Hepatitis B Antibodies Geometric Mean Titer (GMT) at Month 7 (1 month post-dose 3, Stage 2 Infants)

End point title	Anti-Hepatitis B Antibodies Geometric Mean Titer (GMT) at Month 7 (1 month post-dose 3, Stage 2 Infants)[9]

End point description:

GMT is in milli-international units per milliliter [mIU/mL]). A Hepatitis B enhanced chemiluminescence assay was used in this antibody analysis. Per protocol population was defined as the infant participants who met the inclusion criteria, were not protocol violators, were seronegative at baseline (prevaccination anti-HBs titer <5 mIU/mL), and had serology and vaccinations within the specified day ranges.

End point type	Primary

End point timeframe:

Month 7 (1 month post-dose 3)

Notes:

[9] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	112		
Units: mIU/mL				
geometric mean (confidence interval 95%)	6187.7 (5068 to 7554)	4286.1 (3545 to 5182)		

Statistical analyses

Statistical analysis title	Superiority of Anti-HBs GMT Response at Month 7

Statistical analysis description:

Statistical Analysis of Superiority of Anti-HBs GMT Response at Month 7 (1 Month Postdose 3) Between the GSH/2X Phosphate Hepatitis B Vaccine and the 2X Phosphate Hepatitis B Vaccine (Per-Protocol Analysis) – Stage 2

Comparison groups	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants v 2X Phosphate Hepatitis B Vaccine - Stage 2 Infants

Number of subjects included in analysis	222
Analysis specification	Pre-specified
Analysis type	superiority[10]
Parameter estimate	GMT Ratio
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.9

Notes:

[10] - The lower bound of the 95% confidence interval on the GMT ratio greater than the prespecified clinically relevant value of 1.00 (identity) allows for a conclusion of superiority.

Secondary: Percentage of Participants Who Experienced One or More Adverse Events (AEs, Stage 2 Infants)

End point title	Percentage of Participants Who Experienced One or More Adverse Events (AEs, Stage 2 Infants)[11]

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. The safety population consisted of all infant participants who received at least one dose of GSH/2X Phosphate Hepatitis B Vaccine or 2X Phosphate Hepatitis B Vaccine and had follow-up data.

End point type	Secondary

End point timeframe:

Up to 7 months

Notes:

[11] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	119		
Units: Percentage of Participants				
number (not applicable)	76.7	79.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Discontinuing Study Drug Due to AEs (Stage 2 Infants)

End point title	Percentage of Participants Discontinuing Study Drug Due to AEs (Stage 2 Infants)[12]

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether

it is considered related to the medical treatment or procedure, that occurs during the course of the study. The safety population consisted of all infant participants who received at least one dose of GSH/2X Phosphate Hepatitis B Vaccine or 2X Phosphate Hepatitis B Vaccine and had follow-up data.

End point type	Secondary

End point timeframe:

Up to Month 6

Notes:

[12] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	119		
Units: Percentage of Participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Hepatitis B Antibodies Geometric Mean Titer (GMT) at Month 7 (1 Month Post-dose 3, Stage 1 Adults)

End point title	Anti-Hepatitis B Antibodies Geometric Mean Titer (GMT) at Month 7 (1 Month Post-dose 3, Stage 1 Adults)[13]

End point description:

GMT is in milli-international units per milliliter [mIU/mL]). A Hepatitis B enhanced chemiluminescence assay was used in this antibody analysis. Per protocol population was defined as the adult participants who met the inclusion criteria, were not protocol violators, were seronegative at baseline (prevaccination anti-HBs titer <5 mIU/mL), and had serology and vaccinations within the specified day ranges.

End point type	Secondary

End point timeframe:

Month 7 (1 month post-dose 3)

Notes:

[13] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	8		
Units: mIU/mL				
geometric mean (confidence interval 95%)	2127.5 (1177 to 3846)	684.5 (119.2 to 3932)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Elevated Temperatures (Stage 2 Infants)

End point title	Percentage of Participants with Elevated Temperatures (Stage 2 Infants)[14]

End point description:

After each of the 3 vaccinations, participants or the parent/legal guardian (in Stage 2) were to record the participant's temperature in the evening on the day of vaccination and daily at the same time for the next 4 days. An elevated temperature is defined as a rectal temperature of >= 38.1 C (100.6 F) in Stage 2 was considered an adverse experience. The report of a "feverish feeling" was also considered an adverse experience. The safety population consisted of all infant participants who received at least one dose of GSH/2X Phosphate Hepatitis B Vaccine or 2X Phosphate Hepatitis B Vaccine and had follow-up data.

End point type	Secondary

End point timeframe:

Day 1 to Day 5 following any vaccination (Up to approximately 6 months)

Notes:

[14] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	119		
Units: Percentage of Participants				
number (not applicable)	21.7	13.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with One or More Injection-Site AEs (Stage 2 Infants)

End point title	Percentage of Participants with One or More Injection-Site AEs (Stage 2 Infants)[15]

End point description:

Injection-site adverse experiences were observed and recorded for Days 1 through 5 following any vaccination visit for Stage 2. An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that

occurs during the course of the study. The safety population consisted of all infant participants who received at least one dose of GSH/2X Phosphate Hepatitis B Vaccine or 2X Phosphate Hepatitis B Vaccine and had follow-up data.

End point type	Secondary

End point timeframe:

Day 1 to Day 5 following any vaccination (Up to approximately 6 months)

Notes:

[15] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	119		
Units: Percentage of Participants				
number (not applicable)	35	40.3		

Statistical analyses

No statistical analyses for this end point

Secondary: SPR, Percentage of Participants with Anti-HBs Titer ≥10 mIU/mL (Stage 1 Adults)

End point title	SPR, Percentage of Participants with Anti-HBs Titer ≥10 mIU/mL (Stage 1 Adults)[16]

End point description:

SPR is defined as the percentage of participants who demonstrate antibodies to hepatitis B surface antigen ≥10 mIU/mL. A Hepatitis B enhanced chemiluminescence assay was used in this antibody analysis. The statistical criterion for an adequate SPR required the lower bound of the 2-sided multiplicity adjusted 95.0% confidence interval have a lower bound that exceeds 90.0%. Per protocol population was defined as the adult participants who met the inclusion criteria, were not protocol violators, were seronegative at baseline (prevaccination anti-HBs titer <5 mIU/mL), and had serology and vaccinations within the specified day ranges.

End point type	Secondary

End point timeframe:

Month 7 (1 month post-dose 3)

Notes:

[16] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	8		
Units: Percentage of Participants				

number (confidence interval 95%)	95.7 (88.6 to 100)	87.5 (58.2 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Any Quantifiable Anti-HBs (anti-HBs titers ≥ 5 mIU/mL) (Stage 1 Adults)

End point title	Percentage of Participants with Any Quantifiable Anti-HBs (anti-HBs titers ≥ 5 mIU/mL) (Stage 1 Adults)[17]

End point description:

A Hepatitis B enhanced chemiluminescence assay was used in this antibody analysis. Per protocol population was defined as the adult participants who met the inclusion criteria, were not protocol violators, were seronegative at baseline (prevaccination anti-HBs titer <5 mIU/mL), and had serology and vaccinations within the specified day ranges.

End point type	Secondary

End point timeframe:

Month 7 (1 month post-dose 3)

Notes:

[17] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	8		
Units: Percentage of Participants				
number (confidence interval 95%)	97.8 (92.5 to 100)	87.5 (58.2 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with One or More Injection-Site AEs (Stage 1 Adults)

End point title	Percentage of Participants with One or More Injection-Site AEs (Stage 1 Adults)[18]

End point description:

Injection-site adverse experiences were observed and recorded for Days 1 through 5 following any vaccination visit for Stage 2. An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. The safety population consisted of all infant participants who received at least one dose of GSH/2X Phosphate Hepatitis B Vaccine or 2X Phosphate Hepatitis B

Vaccine and had follow-up data.

End point type	Secondary

End point timeframe:

Day 1 to Day 5 following any vaccination (Up to approximately 6 months)

Notes:

[18] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	10		
Units: Percentage of Participants				
number (not applicable)	86	90		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Elevated Temperatures (Stage 1 Adults)

End point title	Percentage of Participants with Elevated Temperatures (Stage 1 Adults)[19]

End point description:

After each of the 3 vaccinations, participants or the parent/legal guardian (in Stage 2) were to record the participant's temperature in the evening on the day of vaccination and daily at the same time for the next 4 days. An elevated temperature is defined as a rectal temperature of >= 38.1 C (100.6 F) in Stage 2 was considered an adverse experience. The report of a "feverish feeling" was also considered an adverse experience. The safety population consisted of all infant participants who received at least one dose of GSH/2X Phosphate Hepatitis B Vaccine or 2X Phosphate Hepatitis B Vaccine and had follow-up data.

End point type	Secondary

End point timeframe:

Day 1 to Day 5 following any vaccination (Up to approximately 6 months)

Notes:

[19] - 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: No statistical analysis was planned or performed for this end point.

End point values	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	10		
Units: Percentage of Participants				
number (not applicable)	2	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 7 months

Adverse event reporting additional description:

The safety population consisted of all participants who received at least one dose of GSH/2X Phosphate Hepatitis B Vaccine or 2X Phosphate Hepatitis B Vaccine. Serious adverse events were reported for the entire study period; non-serious adverse events were reported for Days 1 through 14 following any vaccination.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults

Reporting group description:

Participants will receive a 3 x 10-µg regimen of GSH/2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 1.0-mL intramuscular injection

Reporting group title	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults

Reporting group description:

Participants will receive a 3 x 10-µg regimen of 2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 1.0-mL intramuscular injection

Reporting group title	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants

Reporting group description:

Participants will receive a 3 x 5-µg regimen of GSH/2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 0.5-mL intramuscular injection

Reporting group title	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants

Reporting group description:

Participants will receive a 3 x 5-µg regimen of 2X Phosphate Hepatitis B Vaccine on a 0-, 1-, and 6-month schedule, as a 0.5-mL intramuscular injection.

Serious adverse events	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	1 / 10 (10.00%)	1 / 120 (0.83%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Facial paresis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 10 (10.00%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign intracranial hypertension			

subjects affected / exposed	0 / 50 (0.00%)	1 / 10 (10.00%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 10 (0.00%)	1 / 120 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic arthritis staphylococcal			
subjects affected / exposed	0 / 50 (0.00%)	0 / 10 (0.00%)	0 / 120 (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

Serious adverse events	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 119 (0.84%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Facial paresis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Benign intracranial hypertension			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic arthritis staphylococcal			

subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	GSH/2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	2X Phosphate Hepatitis B Vaccine - Stage 1 Adults	GSH/2X Phosphate Hepatitis B Vaccine - Stage 2 Infants
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 50 (94.00%)	9 / 10 (90.00%)	92 / 120 (76.67%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 50 (8.00%)	0 / 10 (0.00%)	0 / 120 (0.00%)
occurrences (all)	4	0	0
Headache			
subjects affected / exposed	22 / 50 (44.00%)	3 / 10 (30.00%)	0 / 120 (0.00%)
occurrences (all)	42	3	0
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	3 / 50 (6.00%)	1 / 10 (10.00%)	20 / 120 (16.67%)
occurrences (all)	4	2	29
Injection site pain			
subjects affected / exposed	43 / 50 (86.00%)	9 / 10 (90.00%)	17 / 120 (14.17%)
occurrences (all)	110	25	22
Injection site paraesthesia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 10 (10.00%)	0 / 120 (0.00%)
occurrences (all)	0	1	0
Injection site swelling			
subjects affected / exposed	3 / 50 (6.00%)	1 / 10 (10.00%)	15 / 120 (12.50%)
occurrences (all)	3	2	18
Irritability			
subjects affected / exposed	0 / 50 (0.00%)	0 / 10 (0.00%)	30 / 120 (25.00%)
occurrences (all)	0	0	42
Pyrexia			

subjects affected / exposed	3 / 50 (6.00%)	0 / 10 (0.00%)	36 / 120 (30.00%)
occurrences (all)	4	0	43
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 50 (4.00%)	0 / 10 (0.00%)	8 / 120 (6.67%)
occurrences (all)	2	0	10
Nausea			
subjects affected / exposed	3 / 50 (6.00%)	0 / 10 (0.00%)	0 / 120 (0.00%)
occurrences (all)	3	0	0
Teething			
subjects affected / exposed	0 / 50 (0.00%)	0 / 10 (0.00%)	8 / 120 (6.67%)
occurrences (all)	0	0	10
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	3 / 50 (6.00%)	0 / 10 (0.00%)	0 / 120 (0.00%)
occurrences (all)	3	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 50 (4.00%)	0 / 10 (0.00%)	5 / 120 (4.17%)
occurrences (all)	2	0	6
Pharyngolaryngeal pain			
subjects affected / exposed	6 / 50 (12.00%)	1 / 10 (10.00%)	0 / 120 (0.00%)
occurrences (all)	7	1	0
Psychiatric disorders			
Crying			
subjects affected / exposed	0 / 50 (0.00%)	0 / 10 (0.00%)	10 / 120 (8.33%)
occurrences (all)	0	0	15
Restlessness			
subjects affected / exposed	0 / 50 (0.00%)	0 / 10 (0.00%)	4 / 120 (3.33%)
occurrences (all)	0	0	6
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	4 / 50 (8.00%)	0 / 10 (0.00%)	0 / 120 (0.00%)
occurrences (all)	4	0	0
Infections and infestations			

Otitis media			
subjects affected / exposed	0 / 50 (0.00%)	0 / 10 (0.00%)	7 / 120 (5.83%)
occurrences (all)	0	0	7
Rhinitis			
subjects affected / exposed	4 / 50 (8.00%)	0 / 10 (0.00%)	16 / 120 (13.33%)
occurrences (all)	4	0	17
Upper respiratory tract infection			
subjects affected / exposed	3 / 50 (6.00%)	1 / 10 (10.00%)	10 / 120 (8.33%)
occurrences (all)	3	1	12

Non-serious adverse events	2X Phosphate Hepatitis B Vaccine - Stage 2 Infants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	95 / 119 (79.83%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	20 / 119 (16.81%)		
occurrences (all)	25		
Injection site pain			
subjects affected / exposed	18 / 119 (15.13%)		
occurrences (all)	29		
Injection site paraesthesia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Injection site swelling			
subjects affected / exposed	19 / 119 (15.97%)		
occurrences (all)	27		
Irritability			
subjects affected / exposed	39 / 119 (32.77%)		
occurrences (all)	58		

Pyrexia subjects affected / exposed occurrences (all)	27 / 119 (22.69%) 30		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Teething subjects affected / exposed occurrences (all)	 7 / 119 (5.88%) 8 1 / 119 (0.84%) 1 9 / 119 (7.56%) 14		
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)	 0 / 119 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Pharyngolaryngeal pain subjects affected / exposed occurrences (all)	 9 / 119 (7.56%) 9 0 / 119 (0.00%) 0		
Psychiatric disorders Crying subjects affected / exposed occurrences (all) Restlessness subjects affected / exposed occurrences (all)	 10 / 119 (8.40%) 12 7 / 119 (5.88%) 7		
Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all)	 0 / 119 (0.00%) 0		
Infections and infestations			

Otitis media			
subjects affected / exposed	5 / 119 (4.20%)		
occurrences (all)	5		
Rhinitis			
subjects affected / exposed	30 / 119 (25.21%)		
occurrences (all)	32		
Upper respiratory tract infection			
subjects affected / exposed	17 / 119 (14.29%)		
occurrences (all)	18		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported