



Clinical trial results:

A Phase II randomized, open, controlled study of the safety and immunogenicity of GlaxoSmithKline Biologicals' candidate Plasmodium falciparum malaria vaccine RTS,S/AS01E, when incorporated into an Expanded Program on Immunization (EPI) regimen that includes DTPwHepB/Hib, OPV, measles and yellow fever vaccination in infants living in malaria-endemic regions.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2012-005695-34 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 07 October 2009 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 |
| This version publication date | 08 July 2016 |
| First version publication date | 18 July 2015 |
| Version creation reason | <ul style="list-style-type: none">Correction of full data set Data correction due to a system error in EudraCT – Results |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 106369 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00436007 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330 |
| Public contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 208990 4466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 208990 4466, GSKClinicalSupportHD@gsk.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 | 09 July 2010 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 October 2009 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To describe the safety (SAEs) of RTS,S/AS01E when co-administered on a 0, 1, 2-month schedule with DTPwHepB/Hib and OPV at 6, 10 and 14 weeks of age, until 6 months post Dose 3 of RTS,S/AS01E (study Month 8), and when co-administered on a 0, 1, 7-month schedule with DTPwHepB/Hib and OPV at 6 and 10 weeks of age then with measles and yellow fever vaccination at 9 months of age, until one month post Dose 3 of RTS,S/AS01E (study Month 8).

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up for safety events from the time the subject consents to participate in the study until she/he is discharged. Subjects were also followed-up as regards infection with malaria, by passive case detection (PCD). Parents were advised to present their child to a health facility within the study area when he/she was unwell. When a subject was presented to a health facility within a study area, he/she was reviewed by clinically qualified personnel and treated as required. The temperature was recorded and if $\geq 37.5^{\circ}\text{C}$, a blood slide was performed to test for malaria infection. A rapid test was performed to guide immediate patient management, when assessed as needed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 30 April 2007 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 11 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------------------|
| Country: Number of subjects enrolled | Tanzania, United Republic of: 210 |
| Country: Number of subjects enrolled | Ghana: 81 |
| Country: Number of subjects enrolled | Gabon: 220 |
| Worldwide total number of subjects | 511 |
| EEA total number of subjects | 0 |

Notes:

| Subjects enrolled per age group | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 511 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study comprised a vaccination phase (Months 0-8) and a follow-up phase (Months 8-19). The Stamaril™ vaccine was not part of the EPI Tanzanian vaccination schedule at study planning. Hence this vaccine was not administered to subjects from Tanzania.

Pre-assignment

Screening details:

The study comprised a vaccination phase (Months 0-8) and a follow-up phase (Months 8-19). The Stamaril™ vaccine was not part of the EPI Tanzanian vaccination schedule at study planning. Hence this vaccine was not administered to subjects from Tanzania.

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 511 |
| Number of subjects completed | 511 |

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | GSK 257049 1 Group |

Arm description:

Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), Polio Sabin™ and GSK 257049 vaccines at Months 0, 1 and 2, and a single dose of Rouvax™ and Stamaril™ vaccines at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. The Stamaril™ vaccine was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Candidate Plasmodium falciparum malaria vaccine |
| Investigational medicinal product code | RTS,S+AS01E |
| Other name | RTS,S, GSK 257049 |
| Pharmaceutical forms | Powder and suspension for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Intramuscular administration in the left antero-lateral thigh at specified timepoints (see group description details).

| | |
|--|---|
| Investigational medicinal product name | Rouvax |
| Investigational medicinal product code | |
| Other name | AMV, Rouvax™ |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use, Subcutaneous use |

Dosage and administration details:

Intramuscular administration in the left arm at specified timepoints (see group description details).

| | |
|---|---|
| Investigational medicinal product name | Stamaril |
| Investigational medicinal product code | |
| Other name | Yellow Fever Vaccine (YFV), Stamaril™ |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| Intramuscular administration in the right arm at specified timepoints (see group description details). | |
| Investigational medicinal product name | Polio Sabin (Oral) |
| Investigational medicinal product code | |
| Other name | Polio Sabin™, Oral Polio vaccine (OPV) |
| Pharmaceutical forms | Oral suspension |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Oral administration at specified time points (see group description details) | |
| Investigational medicinal product name | DTPw-HBV |
| Investigational medicinal product code | |
| Other name | Tritanrix HepB, Tritanrix™-HepB |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| Intramuscular administration in the right antero-lateral thigh at specified time points (see group description details) | |
| Investigational medicinal product name | Hiberix |
| Investigational medicinal product code | |
| Other name | Hib, Hiberix™ |
| Pharmaceutical forms | Powder and solvent for solution for injection/skin-prick test |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| Intramuscular administration in the right antero-lateral thigh at specified time points (see group description details) | |
| Arm title | GSK 257049 2 Group |
| Arm description: | |
| Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), and Polio Sabin™ at Months 0, 1 and 2, 3 doses of GSK 257049 vaccine at Months 0, 1 and 7, and a single dose of Rouvax™ and Stamaril™ at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. Stamaril™ was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania. | |
| Arm type | Experimental |
| Investigational medicinal product name | Candidate Plasmodium falciparum malaria vaccine |
| Investigational medicinal product code | RTS,S+AS01E |
| Other name | RTS,S, GSK 257049 |
| Pharmaceutical forms | Powder and suspension for suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| Intramuscular administration in the left antero-lateral thigh at specified timepoints (see group description details). | |
| Investigational medicinal product name | Rouvax |
| Investigational medicinal product code | |
| Other name | AMV, Rouvax™ |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use, Subcutaneous use |

| | |
|---|---|
| Dosage and administration details: | |
| Intramuscular administration in the left arm at specified timepoints (see group description details). | |
| Investigational medicinal product name | Stamaril |
| Investigational medicinal product code | |
| Other name | Yellow Fever Vaccine (YFV), Stamaril™ |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| Intramuscular administration in the right arm at specified timepoints (see group description details). | |
| Investigational medicinal product name | Polio Sabin (Oral) |
| Investigational medicinal product code | |
| Other name | Polio Sabin™, Oral Polio vaccine (OPV) |
| Pharmaceutical forms | Oral suspension |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Oral administration at specified time points (see group description details) | |
| Investigational medicinal product name | DTPw-HBV |
| Investigational medicinal product code | |
| Other name | Tritanrix HepB, Tritanrix™-HepB |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| Intramuscular administration in the right antero-lateral thigh at specified time points (see group description details) | |
| Investigational medicinal product name | Hiberix |
| Investigational medicinal product code | |
| Other name | Hib, Hiberix™ |
| Pharmaceutical forms | Powder and solvent for solution for injection/skin-prick test |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| Intramuscular administration in the right antero-lateral thigh at specified time points (see group description details) | |
| Arm title | Tritanrix™ HepB/Hiberix™ Group |
| Arm description: | |
| Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), and Polio Sabin™ at Months 0, 1 and 2, and a single dose of Rouvax™ and Stamaril™ at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. The Stamaril™ vaccine was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania. | |
| Arm type | Active comparator |
| Investigational medicinal product name | Rouvax |
| Investigational medicinal product code | |
| Other name | AMV, Rouvax™ |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use, Subcutaneous use |
| Dosage and administration details: | |
| Intramuscular administration in the left arm at specified timepoints (see group description details). | |
| Investigational medicinal product name | Stamaril |
| Investigational medicinal product code | |
| Other name | Yellow Fever Vaccine (YFV), Stamaril™ |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Intramuscular administration in the right arm at specified timepoints (see group description details).

| | |
|--|--|
| Investigational medicinal product name | Polio Sabin (Oral) |
| Investigational medicinal product code | |
| Other name | Polio Sabin™, Oral Polio vaccine (OPV) |
| Pharmaceutical forms | Oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Oral administration at specified time points (see group description details)

| | |
|--|---------------------------------|
| Investigational medicinal product name | DTPw-HBV |
| Investigational medicinal product code | |
| Other name | Tritanrix HepB, Tritanrix™-HepB |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Intramuscular administration in the right antero-lateral thigh at specified time points (see group description details)

| | |
|--|---|
| Investigational medicinal product name | Hiberix |
| Investigational medicinal product code | |
| Other name | Hib, Hiberix™ |
| Pharmaceutical forms | Powder and solvent for solution for injection/skin-prick test |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Intramuscular administration in the right antero-lateral thigh at specified time points (see group description details)

| Number of subjects in period 1 | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group |
|--------------------------------|--------------------|--------------------|--------------------------------|
| | | | |
| Started | 170 | 170 | 171 |
| Completed | 151 | 156 | 148 |
| Not completed | 19 | 14 | 23 |
| Consent withdrawn by subject | 5 | 3 | 4 |
| Physician decision | - | - | 2 |
| Death | - | 1 | 3 |
| Unspecified | - | - | 1 |
| Lost to follow-up | 14 | 10 | 13 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | GSK 257049 1 Group |
|-----------------------|--------------------|

Reporting group description:

Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), Polio Sabin™ and GSK 257049 vaccines at Months 0, 1 and 2, and a single dose of Rouvax™ and Stamaril™ vaccines at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. The Stamaril™ vaccine was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania.

| | |
|-----------------------|--------------------|
| Reporting group title | GSK 257049 2 Group |
|-----------------------|--------------------|

Reporting group description:

Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), and Polio Sabin™ at Months 0, 1 and 2, 3 doses of GSK 257049 vaccine at Months 0, 1 and 7, and a single dose of Rouvax™ and Stamaril™ at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. Stamaril™ was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania.

| | |
|-----------------------|--------------------------------|
| Reporting group title | Tritanrix™ HepB/Hiberix™ Group |
|-----------------------|--------------------------------|

Reporting group description:

Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), and Polio Sabin™ at Months 0, 1 and 2, and a single dose of Rouvax™ and Stamaril™ at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. The Stamaril™ vaccine was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania.

| Reporting group values | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group |
|--|--------------------|--------------------|--------------------------------|
| Number of subjects | 170 | 170 | 171 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 170 | 170 | 171 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: weeks | | | |
| arithmetic mean | 7 | 7.1 | 7 |
| standard deviation | ± 0.97 | ± 1.05 | ± 0.97 |

| | | | |
|--------------------|----|----|----|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 90 | 84 | 78 |
| Male | 80 | 86 | 93 |

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 511 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 511 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: weeks | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 252 | | |
| Male | 259 | | |

End points

End points reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | GSK 257049 1 Group |
|-----------------------|--------------------|

Reporting group description:

Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), Polio Sabin™ and GSK 257049 vaccines at Months 0, 1 and 2, and a single dose of Rouvax™ and Stamaril™ vaccines at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. The Stamaril™ vaccine was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania.

| | |
|-----------------------|--------------------|
| Reporting group title | GSK 257049 2 Group |
|-----------------------|--------------------|

Reporting group description:

Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), and Polio Sabin™ at Months 0, 1 and 2, 3 doses of GSK 257049 vaccine at Months 0, 1 and 7, and a single dose of Rouvax™ and Stamaril™ at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. Stamaril™ was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania.

| | |
|-----------------------|--------------------------------|
| Reporting group title | Tritanrix™ HepB/Hiberix™ Group |
|-----------------------|--------------------------------|

Reporting group description:

Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), and Polio Sabin™ at Months 0, 1 and 2, and a single dose of Rouvax™ and Stamaril™ at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. The Stamaril™ vaccine was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania.

Primary: Number of subjects with serious adverse events (SAEs).

| | |
|-----------------|---|
| End point title | Number of subjects with serious adverse events (SAEs). ^[1] |
|-----------------|---|

End point description:

SAEs were defined as medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Month 0 to Month 8

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | |
|-----------------------------|--------------------|--------------------|--------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 170 | 170 | 171 | |
| Units: Subjects | | | | |
| Subjects with any SAE(s) | 38 | 28 | 33 | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with serious adverse events (SAEs).

| | |
|-----------------|---|
| End point title | Number of subjects with serious adverse events (SAEs). ^[2] |
|-----------------|---|

End point description:

SAEs were defined as medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Month 8 to Month 19

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | |
|-----------------------------|--------------------|--------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 170 | 170 | 171 | |
| Units: Subjects | | | | |
| Subjects with any SAE(s) | 28 | 24 | 27 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against hepatitis B (Anti-HB antibodies).

| | |
|-----------------|---|
| End point title | Concentrations of antibodies against hepatitis B (Anti-HB antibodies). ^[3] |
|-----------------|---|

End point description:

Anti-HB antibody concentrations were expressed as geometric mean concentrations (GMCs) in milli-international unit per milliliter (mIU/mL). The seroprotection assay cut-off was 10 mIU/mL. This outcome only covers results for the GSK 257049 1 Group.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Months 0, 1, 3 and 7

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: Analysis and results presented solely concern the groups as per specified by endpoint description.

| | | | | |
|--|---------------------------|--|--|--|
| End point values | GSK 257049 1 Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 145 | | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HB, Month 0 [N=145] | 12.5 (9.9 to 15.7) | | | |
| Anti-HB, Month 1 [N=133] | 173.4 (131.9 to 228) | | | |
| Anti-HB, Month 3 [N=130] | 1355.7 (1100.6 to 1669.9) | | | |
| Anti-HB, Month 7 [N=137] | 1555.5 (1315.8 to 1839) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against hepatitis B (Anti-HB antibodies).

| | |
|-----------------|---|
| End point title | Concentrations of antibodies against hepatitis B (Anti-HB antibodies). ^[4] |
|-----------------|---|

End point description:

Anti-HB antibody concentrations were expressed as geometric mean concentrations (GMCs) in milli-international unit per milliliter (mIU/mL). The seroprotection assay cut-off was 10 mIU/mL. This outcome only covers results for the GSK 257049 2 Group.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Months 0, 3, 7 and 8

Notes:

[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: Analysis and results presented solely concern the groups as per specified by endpoint description.

| | | | | |
|--|------------------------------|--|--|--|
| End point values | GSK 257049 2 Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 131 | | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HB, Month 0 [N=131] | 9.6 (7.8 to 11.8) | | | |
| Anti-HB, Month 3 [N=119] | 651.2 (541.1 to 783.8) | | | |
| Anti-HB, Month 7 [N=126] | 1133.1 (972.3 to 1320.6) | | | |
| Anti-HB, Month 8 [N=125] | 59813.5 (47050.5 to 76038.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against hepatitis B (Anti-HB antibodies).

| | |
|-----------------|---|
| End point title | Concentrations of antibodies against hepatitis B (Anti-HB antibodies). ^[5] |
|-----------------|---|

End point description:

Anti-HB antibody concentrations were expressed as geometric mean concentrations (GMCs) in milli-international unit per milliliter (mIU/mL). The seroprotection assay cut-off was 10 mIU/mL. This outcome only covers results for the Tritanrix™ HepB/Hiberix™ Group.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Months 0, 3, 7 and 8

Notes:

[5] - 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: Analysis and results presented solely concern the groups as per specified by endpoint description.

| End point values | Tritanrix™ HepB/Hiberix™ Group | | | |
|--|--------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 143 | | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HB, Month 0 [N=143] | 8.7 (7.3 to 10.5) | | | |
| Anti-HB, Month 3 [N=126] | 338 (266.3 to 429) | | | |
| Anti-HB, Month 7 [N=131] | 159.9 (127 to 201.3) | | | |
| Anti-HB, Month 8 [N=133] | 162.4 (127.9 to 206.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of anti-diphtheria (Anti-D) and anti-tetanus (Anti-T) antibodies.

| | |
|-----------------|--|
| End point title | Concentrations of anti-diphtheria (Anti-D) and anti-tetanus (Anti-T) antibodies. |
|-----------------|--|

End point description:

Anti-D and Anti-T antibody concentrations were expressed as geometric mean concentrations (GMCs) in

international unit per milliliter (IU/mL). The seroprotection assay cut-off was 0.1 IU/mL.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Month 3 | |

| End point values | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | |
|--|--------------------|--------------------|--------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 142 | 133 | 142 | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-D | 1 (0.9 to 1.2) | 1.1 (0.9 to 1.3) | 1.4 (1.2 to 1.7) | |
| Anti-T | 2.8 (2.3 to 3.3) | 2.6 (2.2 to 3.1) | 3.7 (3.2 to 4.3) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of anti-polyribosyl ribitol phosphate (Anti-PRP) antibodies.

| | |
|-----------------|---|
| End point title | Concentrations of anti-polyribosyl ribitol phosphate (Anti-PRP) antibodies. |
|-----------------|---|

End point description:

Anti-PRP antibody concentrations were expressed as geometric mean concentrations (GMCs) in microgram per milliliter (µg/mL). The seroprotection assay cut-off was 0.15 µg/mL.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Month 3 | |

| End point values | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | |
|--|---------------------|---------------------|--------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 141 | 132 | 142 | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP | 13.3 (10.5 to 16.7) | 15.7 (12.6 to 19.4) | 18.6 (14.8 to 23.5) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for antibodies against poliomyelitis types 1, 2 and 3 (Anti-Polio 1, 2 and 3 antibodies).

| | |
|-----------------|--|
| End point title | Titers for antibodies against poliomyelitis types 1, 2 and 3 (Anti-Polio 1, 2 and 3 antibodies). |
|-----------------|--|

End point description:

Anti-Polio 1, 2 and 3 antibody titers were expressed as geometric mean titers (GMTs). The seroprotection assay cut-off was 8.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Month 3

| End point values | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | |
|--|-----------------------|------------------------|--------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 136 | 125 | 133 | |
| Units: titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Polio 1 [N=136;125;131] | 463.6 (342.8 to 627) | 485.5 (342.5 to 688.3) | 500 (365 to 684.9) | |
| Anti-Polio 2 [N=135;124;131] | 494 (389.7 to 626.2) | 563.2 (457.3 to 693.6) | 406.8 (329.1 to 502.9) | |
| Anti-Polio 3 [N=135;125;133] | 123.5 (92.1 to 165.6) | 148.7 (112.2 to 197) | 205.1 (156.5 to 268.7) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of anti-Bordetella pertussis toxin (Anti-BPT) antibodies.

| | |
|-----------------|--|
| End point title | Concentrations of anti-Bordetella pertussis toxin (Anti-BPT) antibodies. |
|-----------------|--|

End point description:

Anti-BPT antibodies were measured by enzyme-linked immunosorbent assay (ELISA). Concentrations were expressed as geometric mean concentrations (GMCs) in ELISA unit per milliliter (EL.U/mL). The seropositivity assay cut-off was 15 EL.U/mL.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Month 3

| End point values | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | |
|--|---------------------|---------------------|--------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 139 | 131 | 139 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-BPT | 85.3 (76.8 to 94.6) | 104.4 (94.8 to 115) | 106.5 (96.1 to 118.1) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of anti-measles antibodies.

| | |
|--|---|
| End point title | Concentrations of anti-measles antibodies. ^[6] |
| End point description: | |
| Anti-measles antibody concentrations were expressed as geometric mean concentrations (GMCs) in milli-international unit per milliliter (mIU/mL). The seropositivity assay cut-off was 150 mIU/mL. The analysis was only performed on subjects from the GSK 257049 2 and Tritanrix™ HepB/Hiberix™ groups. | |
| End point type | Secondary |
| End point timeframe: | |
| At Months 7 and 8 | |

Notes:

[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: Analysis and results presented solely concern the groups as per specified by endpoint description.

| End point values | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | | |
|--|---------------------------|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 122 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-measles, Month 7 [N=112;120] | 75 (75 to 75) | 76.2 (73.8 to 78.6) | | |
| Anti-measles, Month 8 [N=119;122] | 1295.2 (1052.1 to 1594.5) | 1299 (1038.8 to 1624.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for anti-yellow fever antibodies.

| | |
|-----------------|---|
| End point title | Titers for anti-yellow fever antibodies. ^[7] |
|-----------------|---|

End point description:

Anti-yellow fever antibody titers were expressed as geometric mean titers (GMTs). The seroprotection assay cut-off was 10. The analysis was only performed on subjects from the GSK 257049 2 and Tritanrix™ HepB/Hiberix™ groups. The analysis was only performed on subjects from the GSK 257049 2 and Tritanrix™ HepB/Hiberix™ groups.

End point type Secondary

End point timeframe:

At Months 7 and 8.

Notes:

[7] - 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: Analysis and results presented solely concern the groups as per specified by endpoint description.

| End point values | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | | |
|--|------------------------|--------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 62 | 64 | | |
| Units: titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-yellow fever, Month 7 [N=41;46] | 5.3 (4.8 to 5.8) | 5.9 (5.1 to 6.9) | | |
| Anti-yellow fever, Month 8 [N=62;64] | 179.2 (135.9 to 236.3) | 183.4 (134 to 250.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of anti-circumsporozoite protein (Anti-CS) antibodies.

End point title Concentrations of anti-circumsporozoite protein (Anti-CS) antibodies.^[8]

End point description:

Anti-CS antibody antibodies were measured by enzyme-linked immunosorbent assay (ELISA). Concentrations were expressed as geometric mean concentrations (GMCs) in ELISA unit per milliliter (EL.U/mL). The seropositivity assay cut-off was 0.5 EL.U/mL. This outcome only covers results for the GSK 257049 1 Group.

End point type Secondary

End point timeframe:

At Months 0, 1, 3 and 7

Notes:

[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: Analysis and results presented solely concern the groups as per specified by endpoint description.

| End point values | GSK 257049 1 Group | | | |
|--|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 153 | | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-CS, Month 0 [N=153] | 0.4 (0.3 to 0.4) | | | |

| | | | | |
|--------------------------|------------------------|--|--|--|
| Anti-CS, Month 2 [N=137] | 86.6 (66.5 to 112.7) | | | |
| Anti-CS, Month 3 [N=131] | 190.3 (154.3 to 234.7) | | | |
| Anti-CS, Month 7 [N=137] | 35.3 (28.5 to 43.8) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of anti-circumsporozoite protein (Anti-CS) antibodies.

| | |
|-----------------|--|
| End point title | Concentrations of anti-circumsporozoite protein (Anti-CS) antibodies. ^[9] |
|-----------------|--|

End point description:

Anti-CS antibodies were measured by enzyme-linked immunosorbent assay (ELISA). Concentrations were expressed as geometric mean concentrations (GMCs) in ELISA unit per milliliter (EL.U/mL). The seropositivity assay cut-off was 0.5 EL.U/mL. This outcome only covers results for the GSK 257049 2 Group.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Months 0, 3, 7 and 8

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: Analysis and results presented solely concern the groups as per specified by endpoint description.

| | | | | |
|--|-----------------------|--|--|--|
| End point values | GSK 257049 2 Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 141 | | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-CS, Month 0 [N=141] | 0.4 (0.3 to 0.4) | | | |
| Anti-CS, Month 3 [N=121] | 57.7 (43.7 to 76.2) | | | |
| Anti-CS, Month 7 [N=127] | 6.1 (4.6 to 7.9) | | | |
| Anti-CS, Month 8 [N=127] | 107.8 (81.1 to 143.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of anti-circumsporozoite protein (Anti-CS) antibodies.

| | |
|-----------------|---|
| End point title | Concentrations of anti-circumsporozoite protein (Anti-CS) antibodies. ^[10] |
|-----------------|---|

End point description:

Anti-CS antibodies were measured by Enzyme-linked immunosorbent assay (ELISA). Concentrations were expressed as geometric mean concentrations (GMCs) in ELISA unit per milliliter (EL.U/mL). The

seropositivity assay cut-off was 0.5 EL.U/mL. This outcome only covers results for the Tritanrix™ HepB/Hiberix™ Group.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Months 0, 3, 7 and 8

Notes:

[10] - 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: Analysis and results presented solely concern the groups as per specified by endpoint description.

| End point values | Tritanrix™ HepB/Hiberix™ Group | | | |
|--|--------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 156 | | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-CS, Month 0 [N=156] | 0.4 (0.3 to 0.4) | | | |
| Anti-CS, Month 3 [N=129] | 0.3 (0.3 to 0.3) | | | |
| Anti-CS, Month 7 [N=132] | 0.3 (0.3 to 0.3) | | | |
| Anti-CS, Month 8 [N=135] | 0.3 (0.3 to 0.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms.

| | |
|-----------------|---|
| End point title | Number of subjects with solicited local symptoms. |
|-----------------|---|

End point description:

Assessed solicited local symptoms were pain and swelling at injection site following vaccination with each of the following study vaccines administered intramuscularly, e. a. the Tritanrix™ HepB/Hib, Rouvax™, GSK 257049 and Stamaril™ vaccines. The numbers of subjects with each of the assessed solicited local symptoms reported were tabulated for each vaccine administered, separately.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 7-day (Days 0-6) follow-up period after any vaccination with the Tritanrix™ HepB/Hib, Rouvax™, GSK 257049 and Stamaril™ vaccines

| End point values | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | |
|-------------------------------------|-----------------------|-----------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 170 | 170 | 171 | |
| Units: Subjects | | | | |
| Pain - GSK 257049 [N=170;170;0] | 126 | 116 | 0 | |
| Swelling - GSK 257049 [N=170;170;0] | 28 | 44 | 0 | |
| Pain - Rouvax™ [N=163;161;159] | 52 | 54 | 47 | |

| | | | | |
|---|-----|-----|-----|--|
| Swelling - Rouvax™ [N=163;161;159] | 20 | 21 | 16 | |
| Pain - Stamaril™ [N=95;94;94] | 2 | 7 | 2 | |
| Swelling - Stamaril™ [N=95;94;94] | 0 | 1 | 0 | |
| Pain - Tritanrix™ HepB/Hib [N=170;170;171] | 127 | 133 | 140 | |
| Swelling - Tritanrix™ HepB/Hib [N=170;170;171] | 47 | 68 | 68 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms.

| | |
|-----------------|---|
| End point title | Number of subjects with solicited general symptoms. |
|-----------------|---|

End point description:

Assessed solicited general symptoms were drowsiness, fever [axillary temperature equal or above (\geq) 37.5 degrees Celsius ($^{\circ}$ C)], irritability and loss of appetite following any vaccination with any of the study vaccines, e. a. the Tritanrix™ HepB/Hib, Rouvax™, GSK 257049, Stamaril™ and Polio Sabin™ vaccines.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 7-day (Days 0-6) follow-up period after any vaccination

| End point values | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | |
|--|-----------------------|-----------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 170 | 170 | 171 | |
| Units: Subjects | | | | |
| Drowsiness | 82 | 97 | 72 | |
| Fever (axillary temperature \geq 37.5°C) | 102 | 95 | 75 | |
| Irritability | 124 | 131 | 118 | |
| Loss of appetite | 68 | 83 | 70 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

| | |
|-----------------|--|
| End point title | Number of subjects with unsolicited adverse events (AEs) |
|-----------------|--|

End point description:

An unsolicited AE is any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Unsolicited AEs were assessed following vaccination with any of the study vaccines, e. a. the Tritanrix™ HepB/Hib, Rouvax™, GSK 257049, Stamaril™ and Polio Sabin™ vaccines.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| During the 30-day (Days 0-29) follow-up period after any vaccination | |

| End point values | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | |
|-----------------------------|--------------------|--------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 170 | 170 | 171 | |
| Units: Subjects | | | | |
| Subjects with any AE(s) | 160 | 161 | 164 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs).

| | |
|---|--|
| End point title | Number of subjects with serious adverse events (SAEs). |
| End point description: | |
| SAEs were defined as medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity. | |
| End point type | Secondary |
| End point timeframe: | |
| From Month 0 to Month 19 | |

| End point values | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group | |
|-----------------------------|--------------------|--------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 170 | 170 | 171 | |
| Units: Subjects | | | | |
| Subjects with any SAE(s) | 57 | 47 | 49 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs: Months [M] 0-19, as specified for each event; Solicited local (per specified vaccine)/general & Unsolicited AEs: 7- and 30-day post-vaccination periods, respectively. "1" was entered as n at risk if a group is not concerned by a specified event.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 13.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | GSK 257049 1 Group |
|-----------------------|--------------------|

Reporting group description:

Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), Polio Sabin™ and GSK 257049 vaccines at Months 0, 1 and 2, and a single dose of Rouvax™ and Stamaril™ vaccines at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. The Stamaril™ vaccine was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania.

| | |
|-----------------------|--------------------|
| Reporting group title | GSK 257049 2 Group |
|-----------------------|--------------------|

Reporting group description:

Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), and Polio Sabin™ at Months 0, 1 and 2, 3 doses of GSK 257049 vaccine at Months 0, 1 and 7, and a single dose of Rouvax™ and Stamaril™ at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. Stamaril™ was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania.

| | |
|-----------------------|--------------------------------|
| Reporting group title | Tritanrix™ HepB/Hiberix™ Group |
|-----------------------|--------------------------------|

Reporting group description:

Subjects aged 6 to 10 weeks at the time of first vaccination received 3 doses of Tritanrix™ HepB/Hib (reconstituted from Tritanrix™ HepB and Hiberix™), and Polio Sabin™ at Months 0, 1 and 2, 3 doses of GSK 257049 vaccine at Months 0, 1 and 7, and a single dose of Rouvax™ and Stamaril™ at Month 7. The GSK 257049 and Tritanrix™ HepB/Hib vaccines were administered intramuscularly in the left and right antero-lateral thigh, respectively. Rouvax™ and Stamaril™ were administered intramuscularly in the left and right arm respectively. Polio Sabin™ was administered orally. Stamaril™ was not administered to subjects from Tanzania as this vaccine was not foreseen at the time to be introduced to the EPI vaccination schedule in Tanzania.

| Serious adverse events | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group |
|---|--------------------|--------------------|--------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 57 / 170 (33.53%) | 47 / 170 (27.65%) | 49 / 171 (28.65%) |
| number of deaths (all causes) | 0 | 1 | 4 |
| number of deaths resulting from adverse events | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute leukaemia (M0 to 8) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| General disorders and administration site conditions | | | |
| Pyrexia (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Pyrexia (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Bronchial hyperreactivity (M0 to 8) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Pneumonia aspiration (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Asthma (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 2 / 170 (1.18%) | 0 / 171 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Thermal burn (M8 to 19) | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 170 (1.18%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Accidental exposure (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Petroleum distillate poisoning (M8 to 19) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis chemical (M8 to 19) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Congenital, familial and genetic disorders | | | |
| Sickle cell anaemia (M0-8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Sickle cell anaemia with crisis (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Cataract congenital (M0 to 8) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sickle cell anaemia with crisis (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 1 / 170 (0.59%) | 0 / 171 (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 |

| | | | |
|---|-----------------|------------------|------------------|
| Nervous system disorders | | | |
| Febrile convulsion (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 4 / 170 (2.35%) | 0 / 171 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Convulsion (M0 to 8) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Convulsion (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile convulsion (M8 to 19) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 2 / 170 (1.18%) | 0 / 171 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia (M0 to 8) | | | |
| subjects affected / exposed | 6 / 170 (3.53%) | 10 / 170 (5.88%) | 10 / 171 (5.85%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 10 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Microcytic anaemia (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Anaemia (M8 to 19) | | | |
| subjects affected / exposed | 6 / 170 (3.53%) | 6 / 170 (3.53%) | 10 / 171 (5.85%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 6 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Microcytic anaemia (M8 to 19) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|-------------------|------------------|------------------|
| Haemolytic anaemia (M8 to 19) subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 | | | |
| Blepharitis (M0 to 8) subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Conjunctivitis (M0 to 8) subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Gastrointestinal disorders | | | |
| Enteritis (M0 to 8) subjects affected / exposed | 1 / 170 (0.59%) | 1 / 170 (0.59%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria (M8 to 19) subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Glomerulonephritis (M8 to 19) subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Gastroenteritis (M0 to 8) subjects affected / exposed | 17 / 170 (10.00%) | 10 / 170 (5.88%) | 14 / 171 (8.19%) |
| occurrences causally related to treatment / all | 0 / 17 | 0 / 10 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Plasmodium falciparum infection (M0-8) | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 5 / 170 (2.94%) | 10 / 170 (5.88%) | 13 / 171 (7.60%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 10 | 0 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pneumonia (M0 to 8) | | | |
| subjects affected / exposed | 11 / 170 (6.47%) | 9 / 170 (5.29%) | 8 / 171 (4.68%) |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 9 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Upper respiratory tract infection (M0 to 8) | | | |
| subjects affected / exposed | 5 / 170 (2.94%) | 4 / 170 (2.35%) | 4 / 171 (2.34%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impetigo (M0 to 8) | | | |
| subjects affected / exposed | 4 / 170 (2.35%) | 0 / 170 (0.00%) | 3 / 171 (1.75%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis (M0 to 8) | | | |
| subjects affected / exposed | 2 / 170 (1.18%) | 2 / 170 (1.18%) | 3 / 171 (1.75%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection (M0 to 8) | | | |
| subjects affected / exposed | 3 / 170 (1.76%) | 2 / 170 (1.18%) | 0 / 171 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media (M0 to 8) | | | |
| subjects affected / exposed | 3 / 170 (1.76%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Acarodermatitis (M0 to 8) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 2 / 171 (1.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis (M0 to 8) | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 170 (0.59%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Bronchopneumonia (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Escherichia urinary tract infection (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Salmonella sepsis (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Acquired immunodeficiency syndrome (M0 to 8) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Extrapulmonary tuberculosis (M0 to 8) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Hydrocele male infected (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Mastoiditis (M0 to 8) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media acute (M0 to 8) | | | |

| | | | |
|---|-----------------|-----------------|------------------|
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Periorbital abscess (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Pharyngitis (M0 to 8) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Rhinitis (M0 to 8) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Skin infection (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Plasmodium falciparum infection (M8 to 19) | | | |
| subjects affected / exposed | 6 / 170 (3.53%) | 6 / 170 (3.53%) | 14 / 171 (8.19%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 6 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia (M8 to 19) | | | |
| subjects affected / exposed | 5 / 170 (2.94%) | 7 / 170 (4.12%) | 7 / 171 (4.09%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 7 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Upper respiratory tract infection (M8 to 19) | | | |
| subjects affected / exposed | 7 / 170 (4.12%) | 4 / 170 (2.35%) | 5 / 171 (2.92%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 4 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis (M8 to 19) | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 7 / 170 (4.12%) | 6 / 170 (3.53%) | 2 / 171 (1.17%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 6 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Impetigo (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 3 / 170 (1.76%) | 3 / 171 (1.75%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis (M8 to 19) | | | |
| subjects affected / exposed | 3 / 170 (1.76%) | 2 / 170 (1.18%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection (M8 to 19) | | | |
| subjects affected / exposed | 3 / 170 (1.76%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 2 / 171 (1.17%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Bronchopneumonia (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Nasopharyngitis (M8 to 19) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 2 / 171 (1.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acquired immunodeficiency syndrome (M8 to 19) | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Dysentery (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Otitis media acute (M8 to 19) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media chronic (M8 to 19) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Pyelonephritis (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Skin infection (M8 to 19) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection pseudomonal (M8 to 19) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Pharyngitis (M8 to 19) | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration (M0 to 8) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 0 / 171 (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 |
| Malnutrition (M0 to 8) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Malnutrition (M8 to 19) | | | |
| subjects affected / exposed | 2 / 170 (1.18%) | 1 / 170 (0.59%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration (M8 to 19) | | | |
| subjects affected / exposed | 1 / 170 (0.59%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Failure to thrive (M8 to 19) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 0 / 170 (0.00%) | 1 / 171 (0.58%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | GSK 257049 1 Group | GSK 257049 2 Group | Tritanrix™ HepB/Hiberix™ Group |
|---|--------------------|--------------------|-----------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 160 / 170 (94.12%) | 161 / 170 (94.71%) | 164 / 171 (95.91%) |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|---|------------------------|-------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 11 / 170 (6.47%) 11 | 19 / 170 (11.18%) 19 | 11 / 171 (6.43%) 11 |
| General disorders and administration site conditions | | | |
| Drowsiness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 82 / 170 (48.24%) | 97 / 170 (57.06%) | 72 / 171 (42.11%) |
| occurrences (all) | 82 | 97 | 72 |
| Fever | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 102 / 170 (60.00%) | 95 / 170 (55.88%) | 75 / 171 (43.86%) |
| occurrences (all) | 102 | 95 | 75 |
| Irritability | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 124 / 170 (72.94%) | 131 / 170 (77.06%) | 118 / 171 (69.01%) |
| occurrences (all) | 124 | 131 | 118 |
| Loss of appetite | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 68 / 170 (40.00%) | 83 / 170 (48.82%) | 70 / 171 (40.94%) |
| occurrences (all) | 68 | 83 | 70 |
| Pain (post DTPw-HBV/Hib vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 127 / 170 (74.71%) | 133 / 170 (78.24%) | 140 / 171 (81.87%) |
| occurrences (all) | 127 | 133 | 140 |
| Pain (post Rouvax vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[1] | 52 / 163 (31.90%) | 54 / 161 (33.54%) | 47 / 159 (29.56%) |
| occurrences (all) | 52 | 54 | 47 |
| Pain (post GSK257049 vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[2] | 126 / 170 (74.12%) | 116 / 170 (68.24%) | 0 / 1 (0.00%) |
| occurrences (all) | 126 | 116 | 0 |
| Pain (post Stamaril vaccination) | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed ^[3] | 2 / 95 (2.11%) | 7 / 94 (7.45%) | 2 / 94 (2.13%) |
| occurrences (all) | 2 | 7 | 2 |
| Swelling (post DTPw-HBV/Hib vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 47 / 170 (27.65%) | 68 / 170 (40.00%) | 68 / 171 (39.77%) |
| occurrences (all) | 47 | 68 | 68 |
| Swelling (post Rouvax vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[4] | 20 / 163 (12.27%) | 21 / 161 (13.04%) | 16 / 159 (10.06%) |
| occurrences (all) | 20 | 21 | 16 |
| Swelling (post GSK257049 vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[5] | 28 / 170 (16.47%) | 44 / 170 (25.88%) | 0 / 1 (0.00%) |
| occurrences (all) | 28 | 44 | 0 |
| Induration | | | |
| subjects affected / exposed | 26 / 170 (15.29%) | 28 / 170 (16.47%) | 29 / 171 (16.96%) |
| occurrences (all) | 26 | 28 | 29 |
| Swelling (post Stamaril vaccination) | | | |
| subjects affected / exposed | 0 / 170 (0.00%) | 1 / 170 (0.59%) | 0 / 171 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 16 / 170 (9.41%) | 21 / 170 (12.35%) | 19 / 171 (11.11%) |
| occurrences (all) | 16 | 21 | 19 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 21 / 170 (12.35%) | 24 / 170 (14.12%) | 24 / 171 (14.04%) |
| occurrences (all) | 21 | 24 | 24 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 21 / 170 (12.35%) | 30 / 170 (17.65%) | 24 / 171 (14.04%) |
| occurrences (all) | 21 | 30 | 24 |
| Rhinorrhoea | | | |

| | | | |
|--|-------------------------|-------------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 19 / 170 (11.18%) 19 | 19 / 170 (11.18%) 19 | 23 / 171 (13.45%) 23 |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 66 / 170 (38.82%) | 66 / 170 (38.82%) | 65 / 171 (38.01%) |
| occurrences (all) | 66 | 66 | 65 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 53 / 170 (31.18%) | 62 / 170 (36.47%) | 71 / 171 (41.52%) |
| occurrences (all) | 53 | 62 | 71 |
| Gastroenteritis | | | |
| subjects affected / exposed | 29 / 170 (17.06%) | 25 / 170 (14.71%) | 32 / 171 (18.71%) |
| occurrences (all) | 29 | 25 | 32 |
| Rhinitis | | | |
| subjects affected / exposed | 16 / 170 (9.41%) | 21 / 170 (12.35%) | 21 / 171 (12.28%) |
| occurrences (all) | 16 | 21 | 21 |
| Pneumonia | | | |
| subjects affected / exposed | 19 / 170 (11.18%) | 11 / 170 (6.47%) | 9 / 171 (5.26%) |
| occurrences (all) | 19 | 11 | 9 |
| Bronchitis | | | |
| subjects affected / exposed | 17 / 170 (10.00%) | 0 / 170 (0.00%) | 21 / 171 (12.28%) |
| occurrences (all) | 17 | 0 | 21 |

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: Results are presented as per number of subjects with available results regarding the specified vaccine(s)

[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: Results are presented as per number of subjects with available results regarding the specified vaccine(s)

[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: Results are presented as per number of subjects with available results regarding the specified vaccine(s)

[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: Results are presented as per number of subjects with available results regarding the specified vaccine(s)

[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: Results are presented as per number of subjects with available results regarding the specified vaccine(s)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 07 September 2007 | <p>The RTS,S/AS01E candidate malaria vaccine is being developed for the routine immunization of infants and children living in malaria-endemic areas as part of the Expanded Program of Immunization (EPI). The RTS,S/AS01E candidate malaria vaccine consists of sequences of the circumsporozoite (CS) protein and hepatitis B surface antigen (HBsAg) with the proprietary adjuvant AS01E (proprietary liposomes, MPL® and Stimulon® QS21 immunostimulants). The vaccine also induces a strong immune response against hepatitis B.</p> <p>Most previous malaria vaccine studies in children have been conducted with the same antigen, but administered with an adjuvant formulation from the AS02 adjuvant system family which consists of an oil-in-water emulsion, MPL® and QS21. The following table details the various vaccine formulations that have been trialed in humans, are ongoing or are planned for human trials.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported